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Development of UK legislation Guidance for Research Medical and In Vitro Diagnostic Devices

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Development of UK legislation Guidance for Research Medical and In Vitro Diagnostic Devices.

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II. DECLARATION

I, Amedeo Patrizio Carena declare that the work recorded in this thesis has been undertaken by myself unless indicated in the text. This work has not been submitted to another institution for the purposes of gaining an award. Where pieces of information from other sources have been used, they have been acknowledged.

Amedeo Patrizio Carena

III. CERTIFICATION

We certify that Amedeo Patrizio Carena has carried out this research, under our supervision, and that he has fulfilled the conditions of the Ordinance 12, so that he is qualified to submit this thesis for the degree of Master of Sciences.

Professor Zhihong Huang Dr Chunhui Li

IV. ABSTRACT

Background: Legislation controls the research, design, development and manufacture of medical devices and in vitro diagnostic devices in the United Kingdom (UK) and the European Union (EU). Organisations working in this field can demonstrate their regulatory compliance to this legislation by being accredited to BS EN ISO 13485 – BS EN ISO 13485:2016 *'Medical devices - Quality management systems - Requirements for regulatory'*[(1)].

The Departments of Medical Physics and Hydatidiform Mole Follow-Up (Scotland) (HMFUS), collectively referred throughout this thesis as M&H, within Ninewells Hospital NHS Tayside are accredited to this standard to allow them to undertake research, design, development and manufacture of medical and in vitro diagnostic devices. This accreditation also enables medical and in vitro diagnostic devices to be European Conformity *(CE)* marked to the appropriate EU directive or regulation[(180)].

Aim: The aim of this project is to ensure academics and third parties collaborating with M&H meet the legislative and regulatory requirements for the development of those medical or in vitro diagnostic devices to be placed within a healthcare environment.

Method: A review of the new Medical Device Regulations (MDR)[(2)], In Vitro Diagnostic Device Regulations (IVDR)[(3)] and UK Medical Devices Legislation[(4)], alongside the requirements of the 2016 revision of the BS EN ISO 13485 standard, to ensure the continuing accreditation within M&H. A case study of the research

project – ‘the ‘Optical Coherence Elastography’ system, will be undertaken to gain an understanding of the regulatory documentation required.

Results: The development of documentation that must be followed by academics and third parties carrying out research and the devolvement within M&H to ensure their projects meet the requirements of the legislation and BS EN ISO 13485:2016 regulatory requirements. This documentation must also be followed by M&H to ensure their projects meet both the legislative and the regulatory requirements.

Conclusion:

1 That the documentation, required to ensure the work in relation to MDR and IVDR devices meets the regulatory and legislative requirements, has been produced.

2 That this documentation, on being reviewed by external auditors, confirms compliance with BS EN ISO 13485

3 When completed, this documentation will show that the OCE system complies with the legislative exemptions after review.

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IX. ABBREVIATIONS USED IN THE THESIS

3D	3 Dimensional
BSI	British Standards Institution
CE	European Conformity
CMR	Carcinogenic, Mutagenic or Toxic to Reproduction
EEC	European Economic Community
EMC	Electro-Magnetic Compatibility
EU	European Union
EUDAMED	European Databank for Medical Devices
FDA	Food and Drug Administration
GHTF	Global Harmonisation Task Force
GS1	Global Standard One
HIBCC	Health Industry Business Communications Council
HMFUS	Hydatidiform Mole Follow-Up (Scotland)
ICCBBA	International Council for Commonality in Blood Banking Automation
IFA GmbH	Informationsstelle für Arzneispezialitäten
IMDD	Implantable Medical Devices Directive
IMDRF	International Medical Device Regulators Forum
INN	International Non-proprietary Name

ISO	International Organisation for Standardisation
IT	Information Technology
IVDD	In Vitro Diagnostic Device Directive
IVDR	In Vitro Diagnostics Device Regulations
M&H	The Department of Medical Physics and the Hydatidiform Mole Follow-Up (Scotland)
MD	Medical Device
MDD	Medical Device Directive
MDR	Medical Device Regulations
MHRA	Medicines & Healthcare Products Regulatory Agency
MPD	Medical Physics Department
MoD	Ministry of Defence
MRI	Magnetic Resonance Imaging
OCE	Optical Coherence Elastography
OCT	Optical Coherence Tomography
PIP	Poly Implant Prothèse
PMCF	Post Market Clinical Follow-up
PMPF	Post Market Performance Follow-up
PRRC	Person responsible for regulatory compliance
PPM	Planned Preventative Maintenance
PSUR	Periodic Safety Update Report

QA	Quality Assurance
QMS	Quality Management System
RD	Research & Development
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SEA	Single European Act
SLD	Super Luminescent Diode
SOP	Standard Operating Procedure
UDI	Universal Device Identifier
UDI-DI	Universal Device Identification – Device Identifier
UDI-PI	Universal Device Identification – Production Identifier
UK	United Kingdom
WI	Work Instruction

Chapter 1 INTRODUCTION

1.1 Motivation and objectives

A white paper, written and subsequently published by Arthur Cockfield, later Baron Cockfield in 1985,[(5)] outlined the measures to be taken to enable the idea of a single European Economic Community (EEC) market to be brought into being. This white paper[(6)] led to the adoption in the EEC of the Single European Act[(7)]. A provision of this Act was that the single market had to be set up by 31st December 1993. The full extent of this Act has still to be fulfilled and is viewed as a work in progress.

The EU single market has four main principles:

- The free movement of Services
- The free movement of People (workers and citizens)
- The free movement of Money/Capital and
- The free movement of Goods.

The free movement of goods requires the removal of customs and trade barriers between countries. A typical trade barrier between two counties, prior to the adoption of the freedom of movement of goods, was to have slightly differing technical standards or regulatory requirements for similar, or even the same, products. Prior to the introduction of the medical device directive and the in vitro diagnostic directive, each EU member state would insist that any such device would have to be tested to their own country's regulations or standards and, thereafter, tested by a body accredited by that country's standards body.

These 'technical' trade barriers would be removed by the implementation of common legislation relating to specific product grouping. The legislation, in the form of directives or regulations, would set out the requirements for specific devices. Further, harmonised standards to be introduced would detail how the regulations or directives were to be met. By conforming to these standards a legal presumption of conformance in the required areas to which the directives or regulations related to would allow the manufacturer a more assured/simpler route to compliance. For further details regarding harmonised standards please see *2.1.6 'ISO, EN, BS and Harmonised Standards'*.

For medical and in vitro devices, three directives[8,9,10] were issued in the 1990's and all have undergone minor amendments and review since they were issued. All three directives have been criticised in a number of areas. For example the possibility of countries interpreting the directives in differing ways, the lack of oversight of the notified bodies carrying out device assessments and a device vigilance reporting system which was not coordinated nor were the reports fully analysed for trends. Two well publicised scandals[111,112] resulting from device failures resulted in the EU commencing a full review of the three directives. The first was the Poly Implant Prothèse, 'PIP'[111], breast implant scandal. This scandal was closely followed by the metal-on-metal hip replacement scandal[112]. This forced the EU member states to work in closer harmony to revise, strengthen and remove many of the weakness or failings of the three directives. The outcome of this full review was the issue/introduction of the two regulations the Medical Device Regulations (MDR)[2] and the In Vitro Diagnostic Device Regulations (IVDR)[3] in 2017. Prior to the issue of these regulations, the EU undertook measures to address the various problems on an interim basis, for example, the reclassification of breast implants[185]; the recommendations detailed in the EU final opinion on metal on metal hip implants and the responses to the comments related to this opinion paper[186]; and the introduction of the updated standard relating to the biocompatibility of medical devices ISO 10993-1:2009[187].

It should be noted that the difference between EU regulations and EU directives is that EU regulations are binding legislative acts which must be applied in their entirety and without interpretation in each country. Whereas, EU directives set out the goals and aims of the required legislation but it is up to each country's legislative process to determine how to enact the directives into their country's laws.

By changing these directives to regulations another criticism was removed i.e. that the directives were not equally applied across the EU.

Directives or regulations may also require devices to be developed and manufactured to an appropriate quality management standard – BS EN ISO 13485:2016[1] for medical devices and both BS EN ISO 13485:2016 and, with the introduction of the In Vitro Diagnostic Device Regulations, EN ISO 15189:2012 [11], for in vitro diagnostic devices. These standards complement the two regulations and provide regulatory compliance for the various management systems required.

Of the original three directives only the in vitro diagnostic device directive defined the controls under which these devices could be designed, developed and manufactured ‘in-house’ for ‘in-house’ use only. Subsequent to the issue of the Medical Device Directive, guidelines[179] were introduced to control the manufacture of devices by a health care institution for use ‘in-house’ only by that health care institution. (A health care institution is a legal entity whose primary purpose is the care or treatment of patients or promotion of public health.) These controls were not stringent, and, in most cases, no external oversight or review was required. With the introduction of the new regulations the control of such work has been considerably increased. For devices manufactured for ‘in-house’ use, that is, solely to be used within the manufacturing NHS Trust or Health Institution, these two new regulations introduced a number of new requirements.

The need to register any device designed, developed and manufactured for ‘in-house’ use with the local competent or designated authority. In the UK this is the Medicines and Healthcare products Regulatory Agency (MHRA).

The proof that the device(s) meets the safety requirements set out in the relevant directive.

That the work is carried out and conforms to an appropriate Quality Management System, (QMS). In the case of medical devices this would be BS EN ISO 13485. In the case of in vitro diagnostic devices this would be EN ISO 13485 and EN ISO 15189.

The Department of Medical Physics and HMFUS (M&H) design, develop and manufacture medical and in vitro diagnostic devices for both ‘in-house’ use as well as devices supplied to third parties. In order to supply these devices to third parties they have to meet the full requirements of the appropriate EU regulation and be CE marked [2, 3].

The QMS used by M&H is accredited or certificated to a number of standards including BS EN ISO 13485:2016 and BS EN ISO 15189:2012. The accreditation to BS EN ISO 13485 was achieved in 2004 to enable the supply of light therapy testing and treatment units to various dermatology centres within the UK. The standard was also required to enable HMFUS to supply reagents, used in an in vitro diagnostic test, to other hospitals within the UK. Since this initial accreditation, the

standard has been revised and even renamed. Each time there has been a revision in the BS EN ISO 13485 standard, the QMS has been amended to accommodate these revisions. The current revision of this standard is BS EN ISO 13485:2016.

Development work, undertaken in collaboration between M&H, educational institutions or other third parties, must also meet the requirements of the M&H QMS, especially if the output of this work is to be used in trials or by clinical/medical staff within NHS Tayside. As this work is regarded as 'in-house' work' it must meet the same regulatory and statuary requirements.

In this thesis, there is a description of the work undertaken to review the requirements of the new MDR and IVDR; the changes introduced to the new 2016 revision of the BS NE ISO 13485 standard and a determination of how these impacted on the QMS implemented by M&H; the documentation used to control medical and in vitro diagnostic device design, development and manufacture; the control of academic and third party collaborative work and the guidelines to be followed by academic and third party's working in collaboration with M&H.

1.2 Content of thesis

There are 7 chapters in this thesis:

Chapter 1 **Introduction**: The purpose and background of this study

Chapter 2 **Literature Review and Background**: An overview of the quality management standards, background to the EU single market and the regulation of medical and in vitro diagnostic devices. This chapter also provides an overview of the University of Dundee's Optical Coherence Elastography (OCE) system and a review of the documentation produced during the development of the device.

Chapter 3 **Update from BS EN ISO 13485:2012 to BS EN ISO 13485:2016**: The work undertaken to ensure the M&H quality management system, accredited to BS EN ISO 13485:2012[(12)], was reviewed and the changes implemented to ensure compliance with BS EN ISO 13485:2016.

Chapter 4 **EU and UK Medical and In Vitro Diagnostic** Device Legislation: A review of the new EU and UK regulations and the work undertaken to ensure that the M&H quality system was compliant with these new regulations.

Chapter 5 **Case study**: The work undertaken on the OCE to enable this system to be placed in 'a near patient' environment. The guidelines drawn up/developed to ensure Academic and Third Party collaboration with NHS Tayside, relating to the design and manufacture of medical and in vitro diagnostic devices, meet the exemption requirements of the legislation.

Chapter 6 **Conclusions**:

The implementation of the new standard to meet the legislative requirements.

The implementation of the documentation for both M&H work and the academic collaboration.

Chapter 7 **Further Work**:

Continuing the review and auditing of our quality system to ensure that it is fit of purpose.

The development of the OCE system to ensure that it functions correctly, meets the service users' needs and that the results produced are fully validated.

Working with the University of Dundee and other academic bodies to ensure that the collaborative work is correctly controlled and documented.

Chapter 2 LITERATURE REVIEW AND BACKGROUND

2.1 History of Standards in industry

It is important to define the meaning of standards in relation to the work being described in this thesis.

The Collins Dictionary defines a 'standard'[13] as:

1. *'A standard is a level of quality or achievement, especially a level that is thought to be acceptable.'*
2. *'A standard is something that you use in order to judge the quality of something else.'*

The Oxford English Dictionary however lists numerous definitions for the word 'standard'[14] amongst which are:

1. Entry 10 – *'An authoritative or recognized exemplar of correctness, perfection, or some definite degree of any quality.'*
2. Entry 12 – '*A definite level of excellence, attainment, wealth, or the like, or a definite degree of any quality, viewed as a prescribed object of endeavour or as the measure of what is adequate for some purpose; 'specifically' the proper or correct quality*.'

2.1.1 Early Standards

The early building constructors used standard moulds to ensure that the sizing of the materials used in their buildings or monuments was precise. In '*The History of Brick*'[15] it details that Roman bricks were made to standard sizes and were inscribed to denote the maker, and later, additional information on the manufacturing dates was included. In '*The Appearance of Bricks in Ancient Mesopotamia*'[16] it describes the history of mud bricks being manufactured in ancient Mesopotamian times. The use of standard building materials and architectural planning in these ancient times is fully discussed by Shamil in '*Evidence of Architectural Planning and the Use of a Standard Unit of Measurement - the "Ubaid cubit" in Mesopotamia*'[17].

2.1.2 Improving Safety and Trade via Standards.

More recently, safety and trade have been the main drivers for the use of standards. The railways are a good example of this. In the early history of the railway system, railway companies and countries used different rail gauges[18]. The proliferation of the gauge sizes was a direct result of the train manufacturers building to their own dimensions. Different gauge sizes were also used to either stop other companies using their track or to stop other countries using the local rail systems to invade their country. The rail gauges[18, 19] of the USA and Canada in the 1800's are an example of this. Once companies and countries started to realise the cost and trade benefits of having standard rail gauges, the move to standardise rail gauges increased. The Railway Regulation (Gauge) Act 1894[20, 21] brought about the standardisation of railway gauges in the UK.

The use of standards and standardisation by the railways is an early example of industrial era governments and companies understanding the importance of standardisation and the use of standards.

Standards have also been used to control trade and merchandise to ensure that goods are purchased to the correct weight, length or specification. The 'balanced beam' method of comparing weights has been in use since the Bronze Age times and many countries, during the ancient times, had standardised weights[22, 23].

Standards, for reviewing quality of work or goods, have been in existence since humans have been paying for goods or work, no matter the method of payment. The standard used to compare goods may not have been a written document but could be to look at, feel, smell or even taste the goods being traded. The same is true today as consumers may purchase goods based on their appearance, texture, smell or taste.

One of the first UK quality standards was the introduction for the quality mark of gold and silver by Edward I of England in the 1300s. This was to ensure the actual content of the precious metals in a given sample[24].

Edward I also appointed William of Wrotham to report on the quality of the construction of warships. Wrotham was one of the first official quality control inspectors of ships[171].

During the 19th century, when the industrial revolution was taking place, there was an increasing need to control the quality of materials being produced so as to

regulate their actual dimensions and physical properties. The standardisation of common parts used in machines and construction allowed these parts to be massed produced and at known standards of dimension and material quality. An example of an early standard in mechanical engineering is the lowly/humble screw and the Whitworth standard of screw threads and dimensions.

Joseph Whitworth (1803-1897) introduced core and external diameters from a practical standpoint using British inch (imperial) sizes. The system proved to be so good that it remains in use up to this day, mainly as the standard used for pipe fittings[25]. The Whitworth screw is detailed in British Standard BS 84:2007[26] , which can be traced back to the original standard of 1840[27,28]. The use of such standard parts allowed manufacturers to produce consistent goods and ensure customer satisfaction. The First World War required manufacturing processes to become more complex with manufacturers employing larger workforces to meet the need to mass produce equipment and munitions for the war effort. The introduction of piece work and payment for the number of items made, led to poor quality goods being produced and passed to the next stage in the production line/process or the end user. To ensure that the quality of parts or the finished product was to the correct standard, full time inspectors were employed to check the items were of the correct workmanship and required quality. The practice of inspection grew between the First and the Second World Wars and soon departments of quality inspection were to be found in many industries. These departments were solely involved in the inspection of goods and workmanship. During World War II, the practice of inspection continues but in some areas, for example, in the manufacture of explosives, the UK government also required the manufacturers to document their work procedures and ensure that all the workforce adhered to these procedures[29]. This produced a number of benefits, including a reduction in premature detonations of explosives[24], thus reducing the loss in workforce lives and a more consistent product being made resulting in the munitions produced being more effective in the field.

2.1.3 Quality Standards

After the Second World War the UK Ministry of Defence, (MoD), continued to use standards to define work procedures and processes. It also used standards to set the required level of product quality, for example UK's Defence Standard 05-21 'Quality Control System Requirements for Industry' and 05-24 'Inspection System Requirements for Industry' and United States Department of Defence MIL-Q-9858 'Military Specification: Quality Program Requirements. The MoD would inspect the work against the documented procedures and processes to determine how well these were being followed. The MoD would also carry out controls on the end product to ensure the required product quality was being met[24]. Until the end of the 1970's this was also the practice in most industries, with the manufacturers carrying out physical visits to suppliers to determine the quality of the procedures and product.

2.1.4 BS 5750 and ISO 9000

During the late 1970's the UK government lead a campaign to promote quality and reliability in all aspects of British life and industry. The slogan for this campaign was "Quality is everyone's business" and in 1981the British Standards Institute (BSI) issued a group of UK standards the BS 9000[172] series for electronic component quality assurance. As a result, when electronic components manufactured to this standard were purchased, these components would not need to be inspected or tested prior to use by the purchaser. This standard started the transition from the buyer, inspecting the goods to ensure they were fit for purpose, to the producer, having the responsibility for ensuring the goods and services they produced being fit for purpose. This transfer of responsibility meant that the previous standards which had required inspection by the buyer of the supplied products and services to ensure they were of the correct quality and standard was no longer required. In 1979 BSI, after consultation with industry, published the BS 5750 series of standards, which included BS 5750-1:1979 standard[30]. This series of standards was proposed to the International Organisation for Standardisation, ISO, in 1979, and eight years later, in 1987, the ISO 9000 series of standards was published [31]. This series of standards has undergone a number of changes and revisions. The current ISO 9000 series consists of ISO 9001:2015[32] / BS EN ISO

9001:2015[33] and two supporting standards ISO 9000:2015 and ISO 9004:2018. BS EN ISO 9000:2015 and BS EN ISO 9004:2018.

Over the years, more industry specific quality management standards have evolved. These standards have used as their starting point the ISO 9000 standards and added extra requirements or demanded more stringent controls than those required by the ISO 9000 standards. In the USA, their US QS 9000 standard was introduced by the automotive industry in 1994 [34, 35]. This standard has now been superseded to enable component manufacturers having factories in many countries, to manufacture and supply parts to car building plants worldwide using ISO/TS 16949 [36, 37].

Other such standards currently used include AS9100 for the Aerospace Industry[38] and ISO 13485 for the Medical Device Industry[1].

The recent history of the ISO 9000 standard, and its offshoots, have gone through a number of revisions. Some of these have been to remove the military style of language used in the earlier standards while others have been to align the standard with the ideas of Total Quality Management, Risk Management and Process Management. In other words, standards have now evolved from simply looking at how a product is manufactured but to overseeing the whole management structure of an organisation, how the organisation ensures it can meet the present and future needs of its customers and whether or not the organisation reviews its processes and procedures to ensure the customer receives the best product or service possible[39].

The follow excerpt from the QCS International training materials for their 13485 internal auditors training course[40] summarises these changes as follows:

‘Inspection - ie sorting the good from bad. It is estimated that 15% of defective items still pass through an inspection stage.

Quality Control - Planning inspection operations at key stages of the production cycle. This helped to identify errors earlier, but did not prevent them.

Quality Assurance - Meeting customer requirements is the main objective of any organisation. By meeting these requirements, problems can be anticipated and prevented, giving greater confidence to the customer.’

2.1.5 Standard for Medical and In Vitro Diagnostic Design and Manufacture

It should be understood that those producing devices or items under the exemptions given in the UK or EU legislation must still have an 'appropriate' quality management system. The internationally recognised quality management system standard for medical device is ISO 13485. This standard, as EN ISO 13485:2016, is included in the harmonised lists of standards the list of harmonised standards for the IMDD[176], MDD[177] and IVDD[177]. At the time of writing this thesis, there are no harmonised list of standards for the MDR nor the IVDR.

The work described in this thesis relates, in part, to the standard BS EN ISO 13485:2016 – "*Medical devices — Quality management systems — Requirements for regulatory purposes*."[1]. BS EN ISO 13485:2016 is the UK implementation of EN ISO 13485:2016.

The BS EN ISO 13485:2016 standard can be used to show regulatory compliance with EU and UK legislation relating to the design and manufacture of medical and in vitro diagnostic devices. The standard is also being adopted by other national authorities including the USA and Australia[41,42].

A major difference between the two standards is that BS EN ISO 9001:2015 requires 'continual improvement of the quality management system' while BS EN ISO 13485:2016 requires 'maintaining effectiveness of the quality management system' [43,44,45]. Another difference between the two standards is that many of the requirements of BS EN ISO 13485:2016 standard are specific to the design and manufacture of medical devices. These requirements include the need for a file detailing the technical aspects of the device, how the devices are to be manufactured, work environment controls, how the device is to be cleaned or sterilised prior to shipment, stringent controls on the design, development and manufacturing processes and a fully documented process for gathering information related to product feedback once devices have been put into use.

2.1.6 ISO, EN, BS and Harmonised Standards

An ISO standard is an internationally agreed standard, EN standards are those ISO or, other standardisation body, standards transposed for use within the EU or developed by a standardisation institute, nominated by the EU, to meet the needs of a specific EU directive or regulation(188). The original standards may have minor changes made to them to ensure that they meet EU requirements. These harmonised standards will, as required, include information detailing how the standards can be used to show conformance to one or more EU directive or regulation. Where required a list of harmonised EN standards will normally be published to support an EU directive or regulation. BS standards are those translated into English and for use within the UK. Thus, the main text, contained in either an EN or BS standard will be the same as the original standard. The main difference will normally be the inclusion of annexes detailing how the standard can be used to demonstrate conformance to EU regulations or directives.

To meet the requirements of an EU directive or regulation it is necessary to implement only those areas of a standard relevant to the device or service being designed. If a harmonised standard is available, then, that is the preferred document to prove compliance to the requirements of the EU legislation(189). If there are no relevant standards, then other documentation may be referenced in showing how the device or service meets the requirements of the EU legislation for example Common Specifications and Common Technical Specifications(190).

2.1.7 BS EN ISO 13485:2016 and 'In-House' Manufacture

Devices or items for 'in-house' use, under the exemptions given in the UK or EU legislation, must still be manufactured under an 'appropriate' quality management system. This, in my opinion can only be the BS EN ISO 13485:2016 standard due to it being the only quality management standard listed in the harmonised standards list for IMDD, MDD and IVDD. BS EN ISO 13485:2016 does not fully meet the requirements of MDR, or, the IVDR(191,192). It should be noted that relevant parts of BS EN ISO 15189:2012 is explicitly stated in the exemptions given in the IVDR and the UK legislation. This would the appropriate standard to follow, when required, during the 'in-house' manufacture of in vitro diagnostic devices.

Currently, M&H carry out design and development of medical and in vitro diagnostic devices. The M&H QMS has been accredited to BS EN ISO 13485:2016 standard to ensure the work undertaken to manufacture 'in-house' devices meets the requirements of current legislation. Additionally, academics or third parties working in collaboration with M&H must also adhere to all of the M&H QMS.

The actions taken to ensure the M&H QMS fully complies with the 2016 revision of this standard are detailed in *Chapter* 3 '*Update from BS EN ISO 13485:2012 to BS EN ISO 13485:2016*'.

2.2 Medical and In Vitro Diagnostic Device regulation and legislation

The current EU and UK legislation dates back to the mid-1980s when the concept of the single market was introduced and finally resulted in the issue of the Single European Act (SEA)[7]. This Act sought to reduce the trade barriers between the member states of the European Economic Community (EEC) as detailed in the White Paper of 14th June 1985 entitled 'Completing the Internal Market'[6]. This paper detailed numerous barriers to trade and how their removal would benefit trade between member states of the EEC. Medical and in vitro diagnostic devices were included in this white paper. The following outlines the history of the medical device directives and why these directives became regulations.

2.2.1 The three directives.

In the late 1980 three directives were proposed:

1. The Active Implantable Medical Device Directive - 90/385/EEC of 20 June 1990(8);
2. The Medical Device Directive - 93/42/EEC of 14 June 1993(9), and
3. The In Vitro Diagnostic Device Directive - 98/79/EC of 27 October 1998(10).

In comparison to the previous legislation relating to Medical Devices, namely the Council Directive 84/539/EEC[48], these three directives increased the controls placed on manufacturers and introduced the need to have notified bodies, (93/465/EEC)[49], review various aspects of the manufacturers' work and the designed medical device. The standards also required each country's competent authority to be responsible for medical devices in their country. All this was to ensure that any device placed on the EU market, conformed to one of these directives, would be safe, fit for use, met minimum standards of safety, were designed to agreed standards and had been manufactured under a suitable quality system.

The three medical device directives are termed new approach directives. The following is a review of the requirements of these new approach directives and the controls placed on manufacturers and EU states.

2.2.2 EU Legislation Basics.

In summary, the production of legislation in the EU follows the following steps[(50)]:

Proposals for legislation normally come from the EU commission, which comprises one commissioner from each of the EU countries. These commissioners are delegated by each EU member state's parliament. The proposal may come from interested parties within the EU, EU member states or the EU Parliament.

All proposals are reviewed for their validity by reviewing their economic, social and environmental impact to determine their advantages and disadvantages. The assessment is carried out with interested parties including industry groups and scientific, technical and professional bodies.

The legislation is drafted[(51)] and then passed to the EU Parliament and Council for scrutiny and discussion.

If the legislation is approved by both the EU Parliament and the Council, it is given assent and enacted. This, in turn, may require EU member states having to draft corresponding domestic legislation for their own country's use.

If either the EU Parliament or Council require the documentation to be amended, or agreement cannot be reached, a secondary group arbitrate between the differing views to reach a consensus opinion. The legislation is passed back to the EU Parliament and Council for review.

2.2.3 Layout of EU legislation

The layout of EU legislation relating to directives and regulations follows the guidance given in the 'Joint Practical Guide of the European Parliament, the Council and the Commission for persons involved in the drafting of European Union legislation'[(51,52)]. Briefly the layout is as follows:

1. Title of the Legislation.
2. If required, a Preamble made up of Citations and Recitals.
    a. Citations define the legal basis of the legislation – primary and secondary legislation directly related to the legislation in question. Citations may also detail the main steps in the production of the legislation.
    b. Recitals set out reasons for the provisions of the legislation and the enacting terms contained in it.

3. Articles are the enacting terms of the legislation. Articles may call up specific Annexes as required.
4. Annexes which detail technical requirements or rules to be followed to enable the enacting terms to be met.

2.2.4 History of Medical Device and In Vitro Device Directives

In 1972 the '*Proposal for a Council Directive on the approximation of the laws of Member States relating to electromedical equipment*'[53] was issued. The preamble details the need for goods across the common market to be controlled. The proposal concludes with the following:

'Electromedical devices must be designed and manufactured to a 'high and clearly-defined standard of safety'

To maintain the safety of the device, individual states have imposed their own 'mandatory specifications relating to the technical safety regulations and the inspection procedures'.

The requirements for the standards to be followed during the development and manufacture of device, and the standards themselves, varied from state to state. The variations are barriers to trade. If common standards for these devices were adopted these trade barriers could be reduced or removed.

The common standards will be determined by the International Electrotechnical Commission. By following these standards, manufacturers could show conformity by adding a mark (symbol) to the equipment or via a declaration of conformity attached to the equipment.

The proposal also stated that devices conforming to the proposed directive could still cause a hazard to the user or patients. Hence, it recommended that any member state, finding such a device, may remove it from the market and they must also inform the other members of the community of the reasons for doing so.

The 11 articles contained in the proposed document establish the basis of the modern medical and in vitro device directives and regulations. This document defines medical and in vitro diagnostic devices, the use of harmonised standards to ensure that these are designed, manufactured or produced to international, rather than single country standards, and the need to report medical and in vitro devices

found to be unsafe or defective. The proposal also details the need for member states to be satisfied that the device meets the requirements. As previously stated, to confirm that this has been achieved, a mark can be added to the device or a declaration of conformity issued with the device.

It should be noted that that there are two unnamed Annexes attached to the proposal. The first annex relates only to the proposal for electro medical equipment and details a list of devices exempt from the requirements of the proposal. The second annex details a template for a certificate and a proposed mark of conformity.

The proposal was reviewed, as detailed in 'Opinion on the proposal for a Council Directive on the approximation of the laws of the Member States relating to electro-medical equipment'[(56)]. This document details how the report was submitted to various committees for review and comment, along with a report written by Rapporteur, Sir John Peel, UK[(56)], on the proposal. The outcome of the review was that various changes were required to be made to the proposals. These changes were as follows:

The devices which were excluded and listed annex 1 above, were there due to a lack of technical standards. Many of these exclusion could be removed once harmonised standards were issued.

There was a lack of detail relating to the training of device users and the place of use of the equipment required to be addressed.

Manufacturers should not be allowed to apply to more than one member state to have their device approved. In addition, there was a lack of clarity on who should authorise the conformity of a device; was it is to be a manufacturer or an 'approved laboratory'.

The time scales for the introduction of the proposed directive was noted to be rather short and should be reviewed in light of the required work to produce the necessary harmonised standards, allow manufacturers to test equipment to these new standards and for the setting up of appropriate reporting structures.

The proposed directive was eventually issued, nearly ten years later, as the 'Council Directive 84/539/EEC of 17 September 1984 on the approximation of the laws of the Member States relating to electro-medical equipment used in human or veterinary medicine'[(48)]. The Directive consisted of nine pages, a preamble, eleven

legislative articles and four annexes. The main thrust of the directive was to reduce or remove barriers to trade by adopting common standards for equipment safety and design. In contrast to the original negative style, the issued directive was written in a positive style, detailing inclusions rather than exclusions, stating matters that shall be done rather than maters not to be done and allowance for devices not covered by written standards. The articles of the directive have been expanded to give greater clarity but with no real change to the legal aspects of the directive when compared to the original proposal and requested changes. The four annexes associated with this directive detailed the technical requirements to be followed, a comprehensive list of devices included within the scope of the directive, the layout of the mark of conformance and a specimen of the declaration of conformance.

During the 1990's, the requirements relating to medical devices contained in directive, 84/539/EEC[48], were replaced by Directives 90/385/EEC[8] and 93/42/EEC[9].

The proposal[57] for Directive 90/385/EEC on active implantable medical devices was issued in December 1989. The directive, '*The Active Implantable Medical Devices Directive*, the IMDD, was then issued in June 1990. The reason for the introduction of this directive was to address the fact that there were no harmonised requirements for Active Implantable devices in the EU and that each member state had drawn up their own testing and safety requirements. (The route from the proposal to adopted legislation is available by reviewing the procedure tab of the proposal document[58].)

The proposal for amending Directive 84/539/EEC was issued in August 1991[59] and its replacement, Council Directive 93/42/EEC[9] was issued in June 1993. This directive was commonly known as the Medical Device Directive or MDD. (The timeline from proposal to adopted legislation is given in the procedure tab of the proposal document[60].) The new directive was issued to address a number of issues arising from the experience gained in the application of the 84/539/EEC directive.

The final directive was Directive '*98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices*', IVDD,[10]. This directive was officially proposed in 1995[61] and, from proposal to adoption as a full

EU directive, took over five years[62]. This directive was introduced as there were no specific requirements for such devices in the EU.

In the veterinary field, Directive 84/539/EEC[48] was finally repealed in 2008[63] with the publication of a directive specifically for electro-medical equipment used in veterinary medicine.

2.2.5 Overview of the Three Directives – IMDD, MDD and IVDR

The key changes to the regulations controlling the design and manufacture of medical and in vitro devices following the issue of these new directives are:

2.2.5.1 Implantable medical device directive - 90/385/EEC

The proposal for, and subsequent issue of, the IMDD directive introduced a number of new concepts in EU device regulation. Some of these included:

a) Separate definitions for medical devices, active implantable electromedical devices and permanently implanted devices;
b) Defined assessment criteria for notified bodies carrying out assessments of implantable, medical and in vitro diagnostic devices and their manufacturers;
c) Defined schemes to assess conformity of product design and manufacture to the appropriate directive;
d) Specified essential requirements, for device safety, device design, device technical files and the information to be provided to device users;
e) The concept that any remaining risk must be outweighed by the clinical benefit of using the device;
f) Criteria of how to undertake and report device clinical evaluation; and
g) Controls for custom made or special devices for clinical investigation.

The IMDD was enabled into UK law on 1st January 1993 by the '1992 No. 3146 CONSUMER PROTECTION The Active Implantable Medical Devices Regulations 1992'[64].

2.2.5.2 Medical Device Directive 93/42/EEC.

The proposal for the 1993 Medical Device Directive[59] was written seven year years after the issue of the 1984 Directive 84/539/EEC[48]. The proposal reviewed experience gained, and problems encountered, with the original directive. The new directive maintained the layout and basic requirements of the Implantable Medical Device Directive. The proposal for the MDD included findings from a number of reviews of the medical device sector and gained opinion from national bodies on the effectiveness and implementation of the 1984 Directive[48]. These reviews and opinions showed that the regulation of medical devices varied between member states, the technical harmonisation hoped for had not occurred and the device vigilance also varied between countries thus compromising patient safety. To help improve this, the following new concepts were introduced in directive 93/42/EEC:

a) Four risk categories for medical devices.
b) Definition of in vitro diagnostic device as separate from a medical device.
c) The amount of intervention by notified and country authorities will depend on the risk category of the device.
d) The proposal allows for combinatorial devices; a medical device which incorporates a medicinal product, and gives clear requirements as to how medicinal products and medical devices are to be regulated.
e) Requirements for systems and procedure packs.
f) Definition of manufacturer and those placing products on the market and their role in device safety is defined.
g) Provisions for devices emitting ionisation radiation are included in the 93/42/EEC directive.
h) Definition of the persons responsible for placing devices on the market and the need for these persons to be registered with the appropriate competent authority.

Due to these extra controls and requirements the published MDD, 93/42/EEC, is 43 pages long while the originally published 1984 directive, 84/539/EEC, was only nine pages long.

The '*1994 No. 3017 CONSUMER PROTECTION The Medical Devices Regulations 1994* '[(65)] passing the MDD in to UK law came fully into force on 1st January 1995.

2.2.5.3 In Vitro Diagnostic Directive 98/79/EC[(10),] IVDD

The need for the IVDD directive is detailed in the proposal document of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices'[(61)]. The proposal clearly defines an in vitro diagnostic device as a device used 'outside the human body for medical examinations of samples taken from the patient'. The samples may be examined in a laboratory, near or at the patient's bedside or by the patient, as and when required. The findings of the various reviews, referenced by the proposal, concluded that member states had introduced their own legislation and, in some cases, specific standards to control the design, manufacture and conformity testing of specific in vitro diagnostic devices. These differences in member states' legislation and controls was hampering the free movement of in vitro diagnostic devices, even if these devices were performing the same tests, in the same manner, as others already placed on the market. The proposal acknowledges that some in vitro diagnostic devices would be used for self-testing and details special requirements to ensure their safe and correct use by those with little, or no knowledge, of how the device actually works. All of the requirements detailed in the proposal were included in the published Directive.

The UK legislation, relating to the IVDD, was '2000 No. 1315 CONSUMER PROTECTION The In Vitro Diagnostic Medical'[(66)].

The three directives were not without their problems and all three were reviewed, repealed and replaced by two regulations – the Medical Device Regulations, MDR, (EU) 2017/745 [(2)], which combined and replaced both the IMDD and the MDD and the In vitro Diagnostic Device Regulations, IVDR (EU) 2017/746[(3)] which had replaced the IVDD. Chapter 4 '*EU and UK Medical and In Vitro Diagnostic Device Legislation*' details' the main differences between the old directives and the new regulations. The main point to note is that unlike directives EU member states must enact the regulations with no interpretation.

2.2.6 'In-House' manufacture and control

Previous to the publication of the IMDD and MDD, health care institutions were able to carry out 'in-house' manufacture or modify existing medical devices, active implantable devices or in vitro diagnostic devices to ensure effective patient care and allow medical, clinical and laboratory staff to undertake their duties appropriately without restrictions. Examples of this include adapting medical devices to match patient anatomy, manufacturing an IVDD reagent to enable a specific test or producing a specialist surgical tool.

Neither the IMDD nor the MDD had an exemption to allow 'in-house' manufacture, and once these directives were enacted into UK law[64,65], no 'in-house' manufacture was allowed within health care institutions. This problem was circumvented by the Bulletin 18A 1996 issued by the UK Medical Device Agency, now part of The Medicines and Healthcare products Regulatory Agency, (MHRA). This bulletin, which became EU guidance, detailed the view that devices made solely for use within a single legal entity were not placed on the market and hence did not come under the remit of the MDD. The Bulletin informed that the guidance would also apply to the IMDD. The current revision of this bulletin is given in the MHRA Guidance '*In-House' manufacture of medical devices*'[179].

Bulletin 18A suggests that healthcare institutions may not need to follow any of the guidance detailed in the IMDD or the MDD . This is not the case in the UK and other countries, as the legislation, enacting these directives, was enabled within legislation protecting the rights and safety of the general public. In the UK this legislation is within the general scope of the Consumer Protection Act. This legislation does not differentiate between health care institutions or general industry. Hence, most health institutions deemed it wise to follow the requirements of the directives when undertaking 'in-house' design and manufacture. Within NHS Tayside, the 'in-house' design and manufacture of medical and in vitro diagnostic devices follows the essential safety requirements and conditions/standards relating to device design and construction. A quality assurance system accreditation to BS EN 46001:1997[67] and subsequently BS EN ISO 13485:2001[68] with regular visits by external auditors who review our quality assurance system, samples of our designs and methods of manufacturing and, on occasion, visit the users of manufactured equipment. The quality system also requires the retention of design

and manufacturing data/documentation for a minimum of five years plus the lifetime of the device after the manufacture of the last such device.

It should be noted that any devices manufactured for third parties, including other health care institutions, must comply with the full requirements of the relevant directives or legislation, the device must be CE marked and accompanied by a certificate of conformance.

After much lobbying by interested individuals, an exemption to enable 'in-house' manufacture of devices was added to the IVDD ('*Scope of the Regulations* para 3 (1) of the UK legislation(66)) prior to its issue.

2.3 Optical Coherence Tomography coupled with Vibrational Elastography

The University of Dundee's School of Science and Engineering, requested that the Medical Physics Department, NHS Tayside, work in conjunction with the University of Dundee to review the Optical Coherence Elastography Research scanning system for compliance to medical and in vitro diagnostic device legislation, to enable it to be used in a clinical area of Ninewells Hospital, Dundee, UK. A review of the documentation for this project will be used to fulfil one of the objectives of this thesis, to determine the type of guidance to be given to academics and third parties, to ensure medical and in vitro diagnostic devices, designed and manufactured, would meet UK legislation.

2.3.1 Background

Patients are often required to attend for minor surgery to obtain biopsy samples to determine if an area of clinical interest requires to be further investigated or removed due to an underlying condition or disease. This area of interest may have been highlighted through visual examination or via a medical imaging technique such as Magnetic Resonance Imaging, (MRI), Ultrasound scanning or Nuclear Medicine Imaging. These imaging techniques can highlight areas of interest but do not normally give a definitive outcome as to what the area of interest might be, for example does the image show a benign cyst, a malignant tumour or just a thickening of the tissue or muscle in the area of interest.

When such an area of interest is found it is common practice for a biopsy sample to be taken. These biopsy samples may be taken with, or without, the use of pain management. They may also be taken using local or general anaesthetic. The samples are sent for specialist laboratory testing and reviewed by a consultant in the field. The NHS Tayside Pathology User Handbook[(69)] details the type of work such a laboratory undertakes and also gives testing and review turnaround times for biopsy samples as between two and nine days, depending on the urgency and sample type.

Reducing this sample testing and review turnaround time would be of great benefit to both the patient and clinical/medical staff. A reduction in turnaround times may, potentially, allow clinical/medical staff to inform the patient as to the clinical

significance of the biopsy, prior to leaving the hospital. If the biopsy is negative, then being able to inform the patient of this fact, within hours instead of days, would reduce anxiety and stress to the patient. If the area of interest is clinically significant, it enables the clinical/medical staff to discuss the results of the biopsy with the patient, review possible treatment scenarios and, if prior consent from the patient has been given, begin treatment prior to the patient leaving the hospital i.e. excise the area of interest, commence chemical or drug treatment to the area of interest or commence any other appropriate course of action.

2.3.2 Optical Coherence Elastography, OCE, – Clinical Need

Devices to speed up the review of such areas of interest whether a biopsy is taken or the area reviewed in vivo would be of great clinical benefit. One such device being developed by the University of Dundee, consists of an optical coherence tomography 'camera' coupled to a vibrational elastography system to analyse biopsy samples. The coupling of these two modes/devices allows the microscopic structure of the sample to be viewed and will determine the physical properties of the sample. This will allow the clinical staff a 'real time' assessment of the biopsy sample. Any areas displaying a stiffer structure will normally denote a probable cancerous growth.

2.3.3 Overview of Optical Coherence Elastography, OCE

The OCE system is an Optical Coherence Tomography scanner coupled with a sample vibration system to enable the elasticity of the sample to be determined.

2.3.3.1 Overview of Optical Coherence Tomography, OCT

Optical Coherence Tomography (OCT), of a tissue sample is basically using the properties of a beam of light reflected from the internal structure of the sample to produce depth and intensity information at the point being scanned. If the beam of light is moved in one dimension over a tissue sample information is obtained of the underlying structure of a slice of the tissue. If multiple slices are then scanned, sequentially, over the whole tissue sample, it is possible to view this as a 3-dimensional (3D) reconstruction of the internal structure of the tissue sample, for example, the retina[(75)]. OCT can produce images to a depth of 2-3mm in tissue with

a resolution of 10-30µm. See Figure 2.1[76] for a comparison of various imaging modalities, their range of resolution and penetration depth.

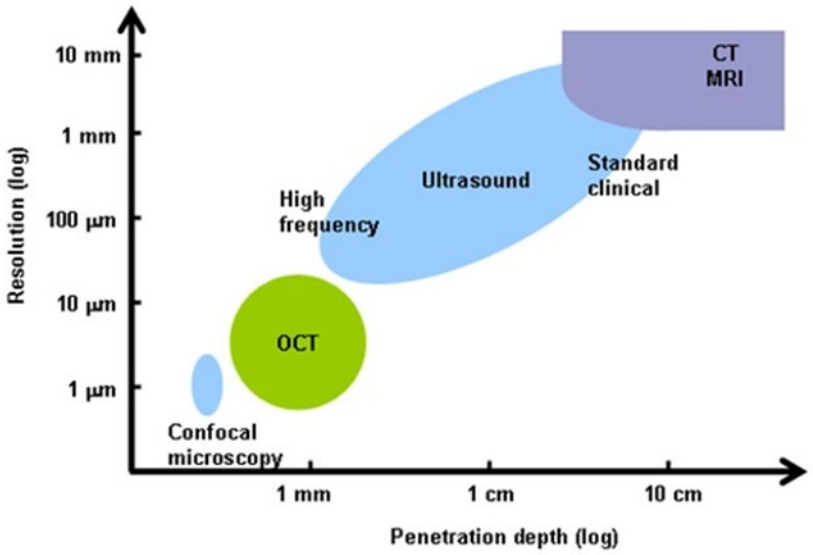


Figure 2.1 Comparison of various medical imaging modalities in terms of resolution and penetration depth[76]

The basic OCT relies on the interference of light. If a beam of light is taken and split into two and the two beams are then recombined, the two beams can be recombined to constructively interfere (add together) or destructively interfere (subtract from each other). This is similar to waves rippling in a pool of water, sometimes they cancel each other out, and at other times they join to make bigger waves. If the effect on the recombination of the two beams of light can be measured to show how they interact then their interference can be measured. A simple interferometer system is given in Figure 2.2[77].

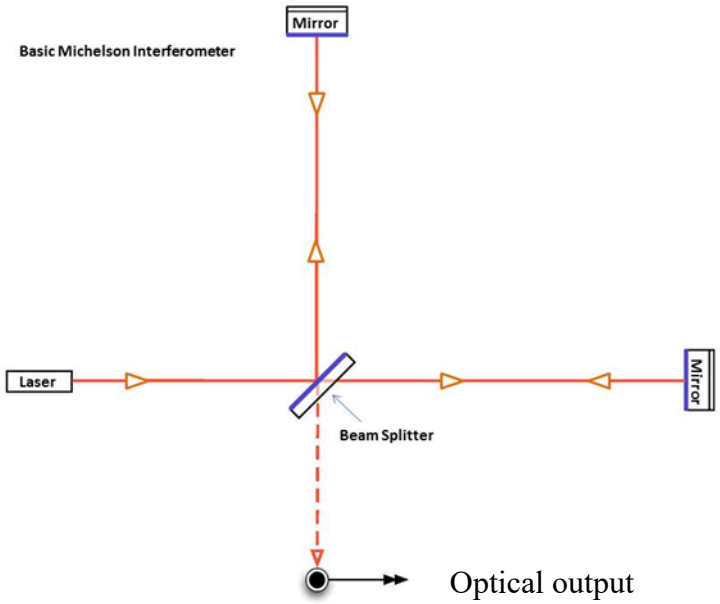


Figure 2.2 Basic Michelson laser interferometer[77].

In the system shown in Figure 2.2, the laser beam is split into two. The split beams then travel to two different mirrors and are recombined and passed to the detector. The output from the detector is dependent on the optical path length taken by each split beam. In the gravitational wave detection system[77] the two beams of light recombine to cancel each other out when the system is in a state of equilibrium – no gravitational wave is passing through the system. If a change in length in either arm occurs, due to a gravitational wave, the two beams of light become misaligned and the signal at the detector is no longer zero. The change in the detector signal will depend on the change in length of the arms. If one of the arms had a tissue sample and the sample was scanned the change in the signal would denote the depth from where the light had been scattered back.

Depending on the type of OCT system 3D images can be captured in real time and at a high scan rate. One method of particular interest is Phase Sensitive OCT using a spectrometer to simultaneously capture multiple wavelengths of light reflected from the sample. The outline schematic of such a system is shown in Figure 2.3[78].

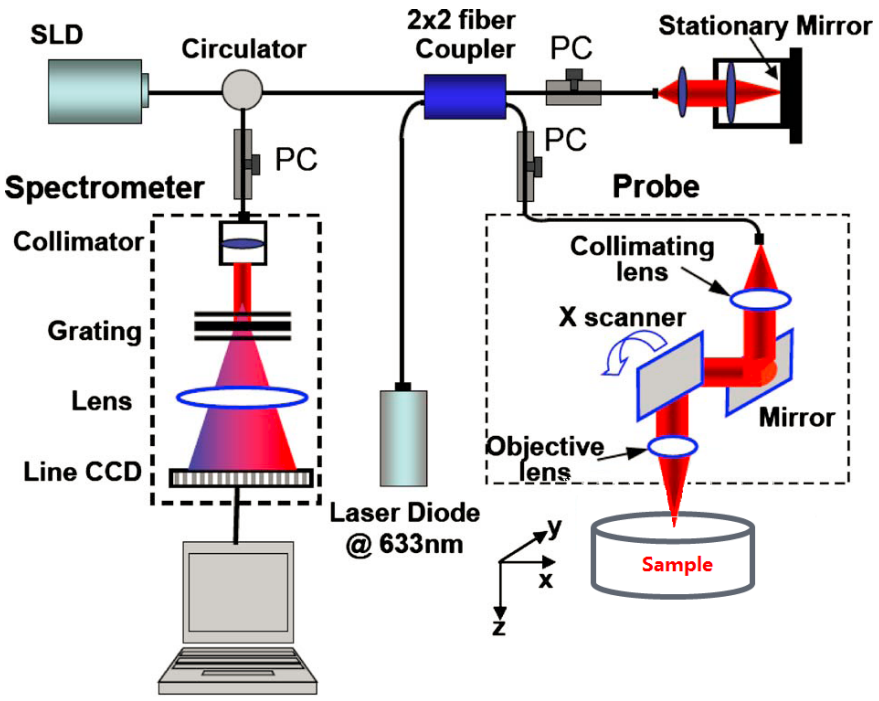


Figure 2.3 Outline schematic of Phase Sensitive OCT[78]

The light source in this OCT system is a broad band super luminescent diode (SLD) so this system uses multiple wave lengths of light. The output from the SLD is split into two beams, one is a reference beam the other is the scanning beam. The scanning of a sample is carried out using a scanning galvanometer system. This type of system enables high speed, high precision scanning of a given sample. The light from the reference and scanning beams are recombined and passed to the optical detector. The optical detector in this case is a type of spectroradiometer. This type of spectroradiometer splits the light into known wavelengths and measures the amplitude of each wavelength simultaneously rather than stepping through each wavelength in turn. This speeds up the scanning of a tissue sample. A computer system then gathers and processes the captured optical and positional date (from the scanning galvanometer) and produces a 3D reconstruction of the sample[75, 78, 79].

The problem with many imaging techniques, including OCT imaging techniques, is that they cannot give any information as to the texture of the sample.

2.3.4 Overview of Elastography

When looking at an area of interest, clinical staff may touch or palpate the area to feel for any abnormalities in the area – is the area softer, harder, does it feel different from the surrounding tissue or organ mass. Normally the area of interest is gently squeezed to determine how it feels in comparison to the remaining tissue or organ. By palpating the area of interest, the specialist is essentially determining the physical properties of the organ. By passing pulses though a material, the movement of the internal structures, due to the vibration of these pulses, will be dependent on their stiffness and density. The pulses may be transmitted in many ways, for example mechanical, ultrasound, laser or even a puff of air. The movement of the internal structures due to these pulses or vibrations can be detected using for example magnetic resonance imaging, ultrasound imaging or optical coherence tomography. The energy imparted by the pulses or the vibrations must be such that the movement of the internal structure is within its normal working limits – the sample should not be damaged due to violent shaking. The duration and speed of the pulses or vibrations is such that the imaging system can see the full range of movement of the internal sample caused by each pulse or vibration. The imaging system must also be able to view the sample to a sufficient depth to be clinically effective. The imaging of tissue stiffness in this manner is known as Elastography. There are a number of wave motions/movements which can be generated within a solid and then analysed to determine the elastic properties of the solid's internal structure[79,80,81]. One of the simplest Elastography methods is the compression method where the sample is either compressed or, for small samples, vibrated on a plate. The deformation of the sample is small to ensure the mechanical properties of the sample are maintained. The change in internal structure gives an indication of the relative stiffness or density of the sample. This information can be used to indicate the histology of the sample.

2.3.5 Optical Coherence Elastography - OCE

To enable the internal structure to be viewed, Optical Coherence Tomography can be used to scan the internal structures of a sample tissue as it is being vibrated to determine its structure, how it reacts to the vibration and hence the elasticity across the sample's volume. – The structure of the sample can be viewed and an indication of the sample's internal stiffness and variation in structural densities can be indicated. This technique is known as Optical Coherence Elastography.

2.3.6 Optical Coherence Elastography commercial devices

From a review of OCE systems on the market, it was found that that use of elastography based ultrasound imaging systems to view and analyse the scanned structure, dominate the market[83,84]. The main areas where examination by Elastography is used are the breast, liver, thyroid, kidney, and lymph nodes.

The two areas where the technique is currently best suited to detect anomalies are the breast and liver areas. The UK National Institute for Health Care Excellence has recommended using elastography as an adjunct to diagnosing breast cancer or liver disease.

Other areas whereby these devices are being used for detection are in the research relating to the review of testicular cancer[70] , tendon injuries [71] and dermatological lesions[74]. Commercial devices have also been developed and placed on the market. For example, the Esaote 'ElaXto: Real-time Elastosonography'[73] can be used to highlight the areas of interest but cannot be used to confirm exactly what the nature of the area of interest may actually be[72].

On reviewing the market for elastography devices, using optical coherence tomography as the imaging modality, it transpires that such devices are mainly used in imaging of the eye and, in particular, the retina[85]. For imaging and diagnosis of biopsy samples, there are many research projects, but no actual commercial devices could be identified by the author during the time of this thesis.

Hence, further development of the University of Dundee OCE system, if successful, could be used as a diagnostic tool which, in turn, would speed up the sample analysis procedure, reduce the time to commence treatment and reduce the cost to carry out the analysis.

2.3.7 Clinical trials and testing of the University of Dundee OCE system.

A clinical trial, ethically approved (ref 2013ON47) comparing the histology of patient biopsy samples was conducted at Ninewells Hospital between April 2014 and December 2015. The trial required the biopsy samples to be taken to the laboratory for scanning on the OCE system and then returned to the urology operating area. The samples were then passed to pathology for review and reporting. This comparison showed that the results from OCE system were on a par with those obtained from the pathology laboratory[79,170].

The next phase of the development of the OCE system is to verify the results of the first trial by scanning a significantly larger number of samples to confirm the results of the initial findings. This second trial (IRAS project ID: 271421) will commence once the COVID-19 situation allows.

To allow such a large number of samples to be scanned, the OCE system will need to be placed within close proximity to the urology theatre area. The work undertaken to review the OCE system to ensure that it was safe and fit for use within the Ninewells Hospital urology theatre, and thus, allow this trial to be undertaken, is detailed in Chapter 5 '*Case study*'.

Chapter 3 UPDATE FROM BS EN ISO 13485:2012 TO BS EN ISO 13485:2016

This chapter is an overview of the work carried out to align the M&H quality system to the requirements of BS EN ISO 13485:2016. This chapter contains the following sections.

1. A brief overview of the changes between the BS EN ISO 13485:2012[(12)] and BS EN ISO 13485:2016.
2. An overview of the M&H quality system
3. The work done with BSI to gain accreditation to the new standard
4. Further review of the M&H quality system against the BS EN ISO 13485:2016 standard.
5. The changes required to bring the M&H quality system in line with the new device regulations.

3.1 A brief overview of the changes between the 2003 and 2016 revisions of the BS EN ISO 13485 standards

It is accepted to be good practice to ensure that the international standards are reviewed to ensure they are still relevant and are kept up to date with current practice, by reviewing them every five years, or more often, if required[(86)]. This five year review interval should be maintained even if only to determine that the standard does not require amendment or revision. A revision period of over five years is deemed unacceptable and, normally occurs, if there are major concerns with the standard under review[(86)].

The review of the 2003 issue of the 13485 standard started in 2012[(87)], a gap of nearly nine years. The revised standard publication was delayed due to various problems including the provisions for the MDR and IVDR and the nonalignment to the standard layout used, for example in the layout used in the ISO 9001:2015 standard[(87,88)]. This delay resulted in the final publication of the revised standard taking place in 2016, a review process of nearly thirteen years.

The review, and final amendment, of the standard had to take into account changes in technology, global regulatory requirements, the evolution and introduction of

new management systems e.g. risk management, tighter control of resource management and the selection and work of subcontractors is now brought fully under the umbrella of the contracting organisation and their management is now based on the risk posed to the contracting organisation and the device to be produced.

Quality management systems have evolved from basic lists of actions, to looking at the complete management system as a set of interrelated processes and how the risk, associated with each process, affects the complete QMS. So, the new standard also had to embrace the process approach used in many other management standards, including ISO 9001:2015. All the management activities are treated as processes, and these processes, are interrelated. Each aspect of the management system will have defined inputs and outputs, and these have a related risk, which must be reviewed and reduced. This was a new concept for the BS EN ISO 13485:2016, but that risk is not confined only to the device but relates to all the processes in the management system.

In addition, the new revision of the standard had to align with the global regulatory requirements of many countries including Brazil, USA and Japan to name just a few.

The standard also introduced the need for the validation of the software used in all aspects of the organisation affecting the QMS, and not just with any software associated with the device or product. This need for software validation is in line with other standards, for example BS EN ISO 17025:2017[(181)] and BS EN ISO 15189:2012[(11)]. Other areas of note are: a new section detailing the manufacturing documentation to be produced; the stricter controls over external suppliers, especially subcontractors; and a greater emphasis on the analysis of the data gathered, during the development of the product and the feedback, once the product is in use. The 13485:2016 standard requires that the implemented quality management system can meet both the customers' needs, the applicable regulatory requirements, and that the responsibility and the authority of the staff, is reviewed and documented[(87,90,91,92,93,94)].

There are a large number of documents detailing the differences between the 2003 and 2016 revisions of the 13485 standard. The documents range from an almost line

by line analysis to those giving a brief overview of the changes. Examples of such documents are given in the references 95, 96, 97, 98 of this thesis and the templates are available in Appendix C3.a1 and Appendix C3.a2.

It has already been noted that there was an update to BS EN ISO 13485:2003[99] released in 2012. This revision is not taken as a global revision of the 13485 standard, but as a European revision[100, 101] of the standard, as detailed in the first paragraph of the forward to the 2012 revision of the standard. This revision adds details on the links between the standard and the three EU medical device directives. These links are fully detailed in annex ZA to ZC of the BS EN ISO 13485:2012 standard. The main body and content of the standard remained unchanged.

3.2 Overview of the M&H Quality Management System[102]

The principal document of the M&H quality system is the M&H Quality Manual. This document details the scope and work of M&H, how M&H controls and manages the work to meet the requirements of these standards. The documentation hierarchy of the M&H quality system is as follows: The M&H Quality manual; M&H quality procedures; protocols, standard operating procedures and work instructions.

Documented quality procedures outline the general tasks and processes related to all areas within the M&H's quality system. These include documentation control, product realisation, internal auditing, purchasing and the disposal of materials and items no longer required.

Specific tasks are detailed in the documentation known as Work Instructions (WI), Standard Operating Procedures (SOP) and Protocols. Examples of these are: WIs detailing specific equipment repair or testing, SOPs relating to the manufacture of reagents and protocols for patient testing.

The M&H quality system must be reviewed, to assess, how changes to relevant legislation, professional body guidance or quality standards affect the quality system and the work undertaken under the QMS.

External assessment of the M&H quality system against the 13485 standards is undertaken by BSI auditors. After initial accreditation to the 13485 standard, BSI

auditors review the quality system over a three-year period, with recertification granted after completion of a successful audit in the third year.

The most recent changes in legislation and the 13485 standard resulted in many change to the M&H QMS. The changes relating to the issue of the BS EN ISO 13485:2016 are fully detailed in the remaining sections of this chapter. Those relating to changes in legislation are detailed in Chapter 4 *'EU and UK Medical and In Vitro Diagnostic Device Legislation'* of this thesis.

3.3 Importance of Accreditation to the new standard

The work undertaken within M&H relies on accreditation to the appropriate quality standards. The HMFUS group requires accreditation to the 13485 standard to supply CE marked in vitro diagnostic devices to hospitals out with NHS Tayside. Both Clinical Engineering and Photobiology manufacture devices for 'in-house' use require accreditation to ensure these devices meet the exemption requirements of the new UK legislation. All certificates to the BS EN ISO 13485:2003/13485:2012 edition of the standard expired on 28 February 2019[182,183]. This date was the end of three-year transition period allowed for companies to become accredited to the new 2016 revision of the 13485 standard. Therefore, without accreditation to BS EN ISO 13485:2016, HMFUS would not be able to supply their in vitro diagnostic device after this date, and all 'in-house' manufacture and associated research, design and development projects could be stopped. Hence, the need to obtain accreditation to BS EN ISO 13485:2016 was vitally important.

3.4 Work to review and update the M&H quality system to meet the requirements of BS EN ISO 13485:2016 standard.

During 2015 and early 2016, various discussions regarding how to manage the transition of the accreditation of the M&H quality system from the BS EN ISO 13485:2012 revision to the BS EN ISO 13485:2016 revision were held with the accreditation body, British Standards Institution, (BSI)[103] and the M&H quality team. The main point arising from these discussions was the transition to the new standard had to be completed, and the M&H quality system reaccredited, by February 2019. Various factors were noted including BSI being short staffed, and the need for them to possibly change auditors and audit dates to ensure that

reaccreditation was achieved by February 2019. In addition, changes to medical and in vitro diagnostic device legislation were being introduced, coupled with the fact that the UK was possibly leaving the EU, and the unknown ramifications this would have on the legislation. (The reality is that the UK has now left the EU but the ramifications to the medical and in vitro diagnostic device legislation are in some ways still unknown.)

At the end of these discussions, it was agreed that, over a period of 24 months, the M&H quality team would carry out a review of the M&H QA manual and documentation against the requirements of the new standard, using the comparison table given in the BS EN ISO 13485:2016 standard, while at the same time, completing the BSI ISO 13485:2016 Readiness Review(104). The M&H quality team would also carry out a review of the new legislation relating to medical devices (as discussed in Chapter 4 *'EU and UK Medical and In Vitro Diagnostic Device Legislation'*). Once these reviews were completed, the M&H team would amend the documentation or produce new documentation, as required. The work was to be completed by the end of 2018 so as to allow BSI to carry out a recertification audit between late 2018 and early 2019.

BSI, on their part, would assist in this process by working with M&H to complete the BSI ISO 13485:2016 Readiness Review. From the results of this review, BSI auditors would amend the audit plans for the next two years, to enable the changes to the current system to be reviewed, in a systematic manner, to determine how well the changes met the requirements of the new standard. After each audit, any audit findings relating to the changed, or new documentation, were to be discussed by the BSI auditor and M&H QA staff to ensure the amendments required were fully understood and the documents were corrected to fully meet the requirements of the standard.

By working in this manner, the M&H quality system should have been able to be reaccredited to the new BS EN ISO 13485:2016 revision by the end of 2018 or early 2019.

3.5 Comparison against 13485 Standard

Table A.1 given in BS EN ISO 12485:2016[(1)] is a comparison of content between the ISO 13485:2003 and ISO 13485:2016 standards. (Remembering that the content and body of BS EN ISO 13485:2012 is the same as the 2003 revision.) This comparison details the major differences between the old and new standards. This comparison, in conjunction with the BSI readiness review, was thought to be sufficient to highlight the required changes to be made to enable accreditation to the new 2016 revision of the standard.

3.6 BSI ISO 13485:2016 Readiness Review

The BSI ISO 13485:2016 Readiness Review, was introduced by BSI to assist organisations in determining how much work they would need to undertake to bring their current 13485:2003 compliant QA systems into line with the new 13485:2016 standard. The Readiness Review was a summary of the changes to the new standard that BSI thought were the most significant. BSI determined that their clients, who were transitioning to the new standard, should review their quality system against the clauses highlighted in the reviews to ensure a smooth transition to the new issue of the standard. As each section of the Readiness Review was completed, amendments, as required to their current quality system to meet the requirements of the new standard, were to be carried out. Once completed, this review was to be submitted to BSI for review and comment. Further scrutiny of this document would form the basis for the various audits leading up to the full re accreditation audit at the end of 2018.

It should be noted that the Readiness Review was compiled by BSI, solely to address the changes to BS EN ISO 13495:2016, it did not take into account the requirements of any EU or UK medical or in vitro diagnostic device legislation.

3.6.1 Comparison Check and BSI Readiness Review - Result

The completed BSI Readiness Review is given in appendix C3-a3 the A summary of the Readiness Review is given in Table 3.1 below. The completed review indicated that M&H either had many of the required elements in place, or that some

documentation required minor amendment to meet the requirements of the updated standard.

From the completed review, it was determined that an update to M&H Quality Manual issue 8(108) was necessary, and a number of quality procedures would be need to be reviewed and amended, as detailed in Table 3.2 Quality Procedures to be Updated. With these documentation changes implemented, it was envisaged by both BSI and the M&H quality team, that the reaccreditation would be obtained

Table 3.1 Summary of completed BSI 13485 Readiness.

13485 Clause	Documentation which requiring to be amended.
Quality Management System Clause 4.1 – General requirements	Role: section 1 (pg 3) QM Regulatory / Risk: 2.2.3, 4.2.1, 5.1, 5.3, 5.5.1, 5.6.2, 6.2.2, 7.1, 7.3.2, 7.5.1 – QM Outsourced: 7.3, 7.5.1 - QM Management: 5.4, 5.6.2, 7.3.7, 7.5, 8.3 - QM Validation: Work Instructions, WI or Standard Operating Procedures SOP required to detail this work.
Quality Management System Clause 4.2 – Documentation requirements	Device File: 7.3 – QM, Updates to QP.02 & associated R&D Work Instructions, 'WI' Documentation: 4.2 – QM Updates to QP.01, QP.24 & associated WI, SOPs, etc.
Management Responsibility Review all clauses	Device File: 7.3, & QP.02 & associated WI's Documentation: 4.2 – QM. And updates to QP.01, QP.24 & associated WI
Resource Management Clause 6.2 – Human resources	Human Resources including training & competence: 6.2 - QM & update to QP.27
Resource Management Clause 6.3 – Infrastructure	Infrastructure: 6.3 – QM only
Resource Management Clause 6.4 – Work environment	Work Environment: 6.4 – QM & QP.30 – both to be reviewed to determine if they need to be updated. Contamination: 6.4.1 – QM Review
Product Realization Clause 7.1 – Planning of product realization	Risk Management: 7.1, 7.3 – QM Storage etc: 7.5 – QM. QP.30, 03, 04, 02 review to determine if update required
Product Realization Clause 7.2 – Customer related processes	Training: 7.2 – QM & QP.27 Communication: 7.2 – QM & QP.02
Product Realization Clause 7.3 – Design and development	Design & Development: 7.3 – QM QP.02 & associated WI's

Product Realization Clause 7.4 – Purchasing7.4	Purchasing: 7.4 - QM & QP.05
Product Realization Clause 7.5 – Production and service provision	Service Provision: 7.5 – QM
Measurement, analysis and improvement Clause 8.2 – Monitoring and measuring	Monitoring & Measuring: 8.2 – QM. QP.35, QP.29 & QP.26
Measurement, analysis and improvement Clause 8.3 – Control of non-conforming product	Non-conforming products: 8.3 – QM. QP.20
Measurement, analysis and improvement Clause 8.4 – Analysis of data	Data: 8.4 – QM
Measurement, analysis and improvement Clause 8.5 – Improvement	Improvement: 8.5 – QM. QP.20

Table 3.2 Quality Procedures to be Updated

Doc No.	Document name.
QP01	Control of Documentation and Data
QP 02	Project Control
QP03	Requirements For Medical Physics Clinical Engineering Services
QP05	Ordering, Receiving and Traceability of Goods and Services
QP20	Reporting and Review of Incidents and Near Misses
QP24	Control of Records
QP26	Customer Feedback
QP27	Competence, Awareness and Training
QP29	Internal Audit
QP30	Handling and storage
QP35	Active Recall Procedure

3.7 Audits Undertaken by BSI and Findings.

The following is a summary of the audits carried out by BSI between June 2016 and October 2018 and the work resulting from these audits carried out.

The reports for the BSI audit mentioned in this section of this chapter can be found via reference (102).

3.7.1 Audit June 2016

During the June 2016 BSI audit, the introduction and implementation of the revised standard was discussed. It was emphasised that M&H would be required to complete the transition to the new 13485 standard by February 2019. The plan proposed by BSI was to continue the cycle of biannual visits, with additional time to review the work undertaken to amend the M&H QMS and assess if these changes met the requirements of the new 13485 standard. Areas identified as 'not compliant' were not documented as an audit non-conformance, as they were outside the scope of the 13485:2003/2012 quality system. These areas of non-conformance were documented as improvement opportunities, and any work undertaken to correct these findings was to be reviewed at the next external audit.

3.7.2 Audit November 2016

The November 2016 audit started to look at the transition to 13485:2016. However, it was also an audit of familiarisation for our BSI auditor who had just been assigned to undertake our audits. The audit highlighted a serious problem with the clinical engineering service process and gaps in the quality system in relation to the new 13485:2016 standard.

These gaps identified that the quality manual did not include reviews of process performance, that product conformity reviews had not be undertaken, that the planned audit schedule was not followed and that changes to the audit schedule were not fully documented.

3.7.3 Audit February 2017

The focus of the February 2017 audit was a review of the M&H quality system against the 9001:2015 standard to determine if the transition to this revised standard could be granted. This accreditation was successful. During this audit, it was

determined that a half day from the following audit would be used to check and complete the readiness review check list and to discuss of the remaining work required to complete the transition.

3.7.4 Audit May 2017

During the May 2017 audit no specific area relating to the 13485:2016 standard was reviewed. The readiness review was completed but not reviewed.

3.7.5 Audit November 2017

During the November 2017 audit, the following areas of the M&H quality system were found to be non-compliant against the 13485:2016 standard:

- The quality manual did not detail the areas of the 13485:2016 standard which were not applicable to this quality system.
- There was no evidence of software validation nor any documentation to control this validation.
- Feedback had been collected, but not annually, as detailed in the controlling work instruction.
- The training received was not reviewed for its effectiveness.
- The temperature of the HMFUS working laboratory was not effectively controlled as the monitoring thermometer was not calibrated.
- The transportation temperature requirements of CE marked products was not defined.

3.7.6 Audit July 2018

The July 2018 audit highlighted the following areas that were not compliant with the standard:

- The preventative and corrective action process was not fully implemented.
- The validation and control of software used by M&H was not fully controlled nor validated prior to use.
- The documentation and process relating to corrective and preventative action required to be fully reviewed.

3.7.7 Audit October 2018

The October 2018 audit was a recertification audit to review the compliance of the M&H QMS to 13485:2016 standard. This audit found that the M&H QMS was compliant to the standard and, as detailed in the report for this audit, the requirements had been effectively implemented and recertification to the new revision of the standard was granted.

Following on from this audit, certification was granted to M&H; certificate FM 77843 against the BS EN ISO 13485:2016 standard.

A number of minor problems were found, these included: a document issued with undeleted draft comments, a lack of knowledge in the use of a/the new equipment asset management system resulting in the planned preventative maintenance (PPM), service and repair scheduling to be adhoc and not fully controlled, an item of safety testing equipment lacked a calibration certificate at the time of the audit and poor control of storage highlighted the need to ensure that items in storage for repair or awaiting delivery were correctly segregated.

3.8 Further review of the M&H quality system against the 13485:2016 standard.

3.8.1 Post Accreditation Audits - 2019

BSI carried out two audits in May and November 2019. The findings of these audits prompted the M&H QA team to carry out another, in depth, review of the M&H quality system against the 13485:2016 standard. The following is a summary of these two audits.

3.8.1.1 May 2019 Audit

This audit, which was the first after the recertification audit, reviewed the M&H quality system against the full requirements of the 13485:2016 standard. During this audit, three minor non-conformities were found. One of, these relating to the procedure controlling design and development, found that this procedure was not fully effective as manufacturing requirements had been detailed.

3.8.1.2 November 2019 audit

This audit reviewed the technical file for a CE marked reagent manufactured by the HMFUS Department, and also, an 'in-house' design project undertaken within the Medical Physics Department.

The audit highlighted a number of areas of concern:

- Data analysis requirements were not fully document.
- Auditing reports lacked relevant details.
- Procedures relating to Complaint Management, Vigilance and Recall/Returns did not include explicit requirements to determine problems with manufactured devices.
- Reporting/analysis of 'in-house' design was not covered in the vigilance reporting procedure.
- The effectiveness of corrective or preventative action was not detailed as required.
- Planning procedures were not fully effective.
- Evaluation of purchased parts was not compliant.

3.9 Second review of M&H Quality system against the BS EN ISO 13485:2016

3.9.1 Rational for second review

As seen in the previous sections, there were numerous problems with the compliance of the M&H quality system against the BS EN ISO 13485:2016 standard as highlighted in the audits carried out in May and November 2019. The problems all related to areas of the M&H system which had been thought to be compliant with the standard and had previously been audited successfully. If these and any other areas of non-compliance, were not correctly addressed, a major non-conformity would have been raised against the M&H quality system with the real possibility of the accreditation to the BS EN ISO 13485:2016 standard being suspended, or even, removed. Thus, the decision of the M&H team to carry out a full review of the M&H quality system against the requirements of the BS EN ISO 13485:2016 was seen as necessary and justified.

3.9.2 Result of the second review

It was determined that the second review of the system against the standard would be a line by line review of the standard against the M&H quality manual. This review is documented in appendix C3.a4 ‘Full review of the present management system against the 13485:2016 standard. (QM issue 10)’.

This second review had highlighted gaps in the M&H quality system to meet the requirements of the 13485:2016 standard.

The documentation to meet the requirements of the design and development clause was lacking, especially the documentation relating to the transfer of the final design to the manufacturing phase. Additionally, there was the need to have separate documentation to control ‘in-house’ manufacture and manufacture of devices made for commercial use.

Post-production and post-market feedback controls did not comply with the requirements of the standard. The procedures at the time only covered ‘CE marked’ devices manufactured by M&H. The controls should have encompassed all devices even those not CE marked.

The standard requires data relating to specific areas of work to be analysed, the analysis does not have to be complex. The controls for the analysis of data were not present in the QA system.

The need to meet regulatory and statutory requirements is not mentioned in the M&H quality manual.

Two requirements of the standard partially covered by the M&H quality system were:

1. the control and monitoring of external contractors to ensure they are fully controlled and evaluated and
4. the inspection of purchased items and services, especially critical items or services, was not correctly documented or recorded.

The second review also highlighted, that by having a standalone technical procedure for medical and in vitro diagnostic device design and manufacture would make the control of such work simpler to understand and control.

In a similar manner, it was seen that a separate technical procedure detailing the work required related to ‘in-house’ manufactured or modified medical and in vitro diagnostic would ensure compliance with the exemption requirements.

There are a number of documents within the M&H quality system used to control and review the design and manufacture of medical and in vitro diagnostic devices. These documents were reviewed to determine if they were still fit for purpose and if new documentation was needed to ensure the M&H quality system meets the required standards and legislations.

Table 3.3 is a list of the pre-existing documentation to be reviewed.

From the review of these documents it was determined that significant amendments were required.

Table 3.4 is a list of the new documentation to be produced to address the requirements of the medical and in vitro device regulations.

Appendix C3.a5 is a summary of the required changes to issue 10 of the M&H quality manual

Table 3.3 Pre-existing documentation to be reviewed

WI Reference	WI Title	Changes Required
WI-RD-01	EC Technical File Contents and Control	Need to amend to include the new requirements of both the legislation and the 13485:2016 standard.
WI-RD-02	Labelling and Instructions for Use Requirements	Need to amend to include new requirements.
WI-RD.03	Product Feedback	Now Post Market Surveillance and greatly expanded.
WI-RD-04	Competent Authority Notification	Similar but greatly expanded plus requirement to include 'in-house' only products.
WI-RD-05	Risk Analysis	Similar but new standard and also requirement to include information from production and post market feedback for lifetime of the device.
WI-RD-10	IVDR Essential Requirements Matrix	Now replaced by General Safety and Performance Requirements
WI-RD-11	MDR Essential Requirements Matrix	Now replaced by General Safety and Performance Requirements
QP.02	Project Control	To be replaced by new QP.02, QP.03F and QP.03G

Table 3.4 New documentation to be produced.

WI Reference	WI Title	Requirement
WI-RD-01	EC Technical File Contents and Control	New requirements for both content and control.
WI-RD-02	Labelling and Instructions for Use	New labelling and instructions for use introduced.
WI-RD.03	Post Market Surveillance	The post market surveillance requirements are new and rather complex.
WI-RD-04	Competent Authority Notification	New requirements and includes 'in-house' developed devices.
WI-RD-05	Risk Analysis	Risk and hazard management requirements increase and new harmonised risk standard issued.
WI-RD-06	Medical Device Classification Rules	Risk classification rules for medical devices changed.
WI-RD-07	In Vitro Diagnostic Devices Classification Rules	Risk classification rules for in vitro device changed.
WI-RD-08	Responsible Person requirements and listing	New UK and EU requirements.
WI0RD-09	UDI Registration, Issue and Allocation	New UK and EU requirements.
WI-RD-10	IVDR General Safety and Performance Requirements Matrix	New UK and EU requirements.
WI-RD-11	MDR General Safety and Performance Requirements Matrix	New UK and EU requirements.
WI-RD-12	Software Development	New UK and EU requirements regarding software development.
WI-RD-13	Testing requirements	New document - to ensure device and manufacturing testing are carried out as per EU and UK legislation and the 13485:2016 standard.
WI-RD14	Planning, Review and Change Control	New document - to ensure planning, review and change control are carried out as required by 13485:2016.
WI-RD-15	Routine Follow-up, Regulatory and Notified Body Communications and Documentation	To include Periodic Safety Update Report, PSUR Post Market Clinical Follow-Up, PMCF and Post-Market Performance Follow-Up, PMPF.

QP.02	Design, Development and Manufacturing not CE marked	Control of work not covered by regulatory or legislative requirements.
QP.03F	Requirements for Product Realisation	Control of work covered by Regulatory or legislative requirements – Medical or In vitro Diagnostic Devices.
QP.03G	Academic and Third Party Product Realisation	Control of work undertaken by academic and third parties on devices which may or may not enter use within NHS Tayside.

Chapter 4 EU AND UK MEDICAL AND IN VITRO DIAGNOSTIC DEVICE LEGISLATION

4.1 Introduction

In 2017, the EU issued the Medical Device Regulations[2] and the In Vitro Diagnostic Device Regulations[3]. These new regulations were issued to rectify a number of failings in the previous legislation and to update the legislation to meet the requirements of new devices, the needs of industry, improve patient safety and ensure better device traceability. Both these regulations were passed into UK law in 2019[4].

4.2 Comparison of the old EU directive and the new EU regulations.

This section is a comparison of the Implantable Medical Device Directive, the Medical Device Directive, and the In Vitro Diagnostic Medical Directive, MDD/IVDD/IMDD against the Medical Device Regulations and the In Vitro Diagnostic Medical Device Regulations, MDR/IVDR. Prior to the UK leaving the EU (Brexit), the UK legislation in respect of Medical Devices and In Vitro Diagnostic Devices mirrored the EU legislation. The main changes in the current UK legislation were the removal of references, where possible, to EU legislation or associated bodies and to substitute these with references to UK legislation or relevant bodies.

The proposals to update and amend MDD, IMDD and IVDD were issued in 2012[105, 106]. These proposals and supporting documentation[129] explain the need for the new legislation, and the reasoning behind the changes, additions and strengthening of the legislation. The new regulations were issued in 2017[2,3].

Examples between the old directives and new regulations include:

The MDD and IMDD are now combined into the MDR. This is to stream line the legislation and ensure that all implantable devices, active or otherwise, are regulated in a similar fashion.

The classification of in vitro diagnostic devices has changed from being list based to risk based[107,108].

The rules for the design and manufacture of medical and in vitro diagnostic device for use within a health care institution have updated been updated and are now stricter. Dependant on use software can now be classified as a medical or in vitro diagnostic device in its own right.

The most important difference is that the legislation is published as regulations and not directives. This means that the new regulations must be applied without change and in their entirety, across the EU. A directive is introduced by each country as they see fit, and devised by their own laws, on how to reach the goals set out in the directive(109).

4.3 Impact on M&H work

The following areas are seen to have the greatest impact on the M&H quality system from these new regulations and UK legislation.

1. The exemptions which allow the manufacture or modification of medical and in vitro diagnostic devices for 'in-house' use only;
2. The control of such projects when working in collaboration with academics and third parties;
3. The replacement of the Essential Requirement, contained in the old directives and UK legislation, with The General Safety and Performance Requirements;
4. The stricter requirements relating to technical file documentation, post market surveillance review and control, hazard and risk management, including the introduction of an updated standard related to risk management.
5. The changes in classification rules.
6. The need to have the appropriate BS EN ISO 15189 certification for in vitro diagnostic devices and how this will impact on the work of the HMFUS group.
7. The new regulations and legislation also introduced the requirement to uniquely identify each manufactured 'CE marked' device, (Universal Device Identifier (UDI) system) and to appoint a responsible person or persons to oversee the regulatory aspects of both the MDR and IVDR against the current M&H quality system.
8. A requirement to have a person or persons nominated to be responsible for regulatory requirements.

9. The need to determine if software is a device in its own right.

Each of the above points will be discussed, and the changes made to the M&H QMS to meet the requirements of the new regulations and legislation, will be detailed in the following sections of this chapter.

4.4 The Exemptions Relating to 'In-House' Manufacturer and Modification

The changes to the exemptions, which allow health care institutions to design and manufacture devices for 'in-house' use, impact on how M&H control and document such work. The exemptions, allowing 'in-house' manufacture and modification detailed in both the EU and the UK legislation[2,3,4] will also affect how the collaborative work with academics and third parties is undertaken.

4.4.1 The Exemptions

Article 5 of both EU Regulations[2,3], 'Placing on the market and putting into service', and the UK legislation[4], 'Placing on the market and putting into service' stated in paragraphs 71 and 140, details the exemptions allowed for the design and manufacture of medical or in vitro diagnostic devices or the modification of existing devices made by a health care institution solely for use within that institution, that is, 'in-house' use. This 'in-house' use relates strictly to devices designed and manufactured solely for the use within the legal authority of the health care facility. The devices may be designed and manufactured with partner organisations but for the sole purpose of use within that specific healthcare organisation. Partner organisations may include universities, technical institutes or subcontracted industrial partners, working in collaboration with a healthcare organisation.

The exemptions are to allow innovation, research and development to be undertaken, while still maintaining patient and user safety. The exemptions detailed in EU and UK legislation are very similar and for clarity, are quoted in appendix C4 1. This similarity is shown in the side by side comparison of the three references given in appendix C4 2. Paragraphs 1 to 5 inclusive are the same apart from the reference to the UK Secretary of State, instead of competent authorities, and the references being made due to the differences in the documentation layout.

The two unnumbered paragraphs after paragraph 5 and referred to as subparagraph 'h)', in the EU legislation equate to UK legislation paragraphs 6, 7 and 8.

Both EU legislation and UK law make provision for more information to be requested, if required, by the relevant EU competent authority or the UK Secretary of State. This extra information would be to allow in-depth scrutiny of a device. The EU Regulations and UK legislation also allow for the restriction of the

manufacture and use of certain devices or device types, even if only for ‘in-house’ use. Hence the need, as detailed in the legislation, to allow for an inspection of the activities of health institutions, to ensure that the requirements of this paragraph and the wider legislation are being followed.

It should also be noted that the manufacture of devices, on an industrial scale is not permitted.

4.4.1.1 ‘In-House’ Exemption Requirement Summary

The following is a summary of the exemption requirements. The paragraph numbers relate to the EU legislation. The differences between UK Law and the EU legislation are noted.

Paragraph 6 relates to the fact that, although the legislation is supposed to be enacted uniformly across all member states of the EU, it may be interpreted slightly differently in some member states. Paragraph 6 allows for the MDR and IVDR to be amended to remove these differences. UK legislation does not need such a paragraph.

Paragraphs 1 to 3 detail that devices that are to be placed on the marked or put into service, must meet the relevant requirements of EU legislation and UK law. The devices will operate as intended, but with the proviso, that they are used and maintained as detailed in the relevant user instructions.

Paragraph 4 states that any device, manufactured and put into use within a health institution, has been placed into service and so the requirements of the legislation apply to these devices.

Paragraph 5 details the requirements to be followed by health care institutions who wish to undertake the manufacture or modification of medical devices only for ‘in-house’ use.

The main condition, as already stated, is that, devices manufactured within a health care institution under these exemptions, is used only within the legal entity of that health care institutions’. For example, if the legal entity comprises a number of hospitals and locations then the device may be used in these hospitals and locations. If devices were transferred to another legal entity, then this would be viewed as placing on the device on the market, and the full requirements of the legislation

would have to be adhered to during the manufacture of the devices. A second condition is that devices are not to be manufactured on an industrial scale. The meaning of industrial is not fully defined in this context. The number of devices manufactured 'in-house' should be compared against the numbers a commercial organisation would be expected to produce of a similar product.

In order to manufacture a new device or modify an existing device, the health institution must justify why currently available devices do not fulfil their needs nor the needs of the relevant patient group. The justification could be that there is no device on the market to meet the relevant clinical requirement, the level of performance or functionality required is not available or the device is meeting a new need not currently addressed on the market. In essence, the exemption is not to manufacture cheaper alternatives for 'in-house' use or to replace existing devices. The exemption is to enable new or innovative devices to be designed and manufactured or existing devices to be modified to fulfil an unmet clinical need.

As previously stated in this thesis, devices are to be designed and manufactured in accordance to an appropriate quality system. For medical devices this is BS EN ISO 13485:2016. For in vitro diagnostic devices this is BS EN ISO 13485:2016 and relevant parts of BS EN ISO 15189:2012. The legislation does not state that the quality system has to be accredited but that the manufacture of the device follows an appropriate quality system. This allows the health institution to implement their own quality system, but they must evidence how their quality system meets the stated requirements. By being accredited to an appropriate industrial standard, it can be seen that best practice is being followed and the stated requirements have been met.

The exemptions, for the actual design and manufacture of a device, require that the device meets the General Safety and Performance Requirements set out in Schedules 3 and 17 (UK legislation) or Annex 1 (MDR and IVDR legislation). Fully documented evidence of how these requirements are met must be available for review. If any of these requirements cannot be fully met, the justification for the discrepancy is to be documented. A statement, confirming why the device is safe to use, must also be given.

To ensure that the device meets the General Safety and Performance Requirements criteria, the use, performance, functionality and manufacturing processes undertaken to produce the device, must be documented. The same documentation must also be produced, to explain how a modification to an existing device has been made, and what, if any, of the original device's functionality has been changed, due to the device modification. The documentation should include a general description of the new medical device or the device modification, the use or purpose of the device or modification and a specification of the device or specification of the modification and how the modification affects the original device's specification. This information must include, the standards which were used in the design and manufacture of the device or modification, the minimum performance criteria, the intended user and patient groups and a risk assessment of the device or modification. There must also be full details of how the device is to be manufactured along with the storage, cleaning and handling requirements. The manufacturing information must include instructions for monitoring, checking, labelling or relabelling and calibrating or testing the device, prior to issuing it to the user. If required, any special instructions on how the device is to be stored or packaged prior to moving or transporting it, should be made available.

The device should be accompanied with relevant user instructions including repair, maintenance, cleaning and calibration details.

The documentation will also detail how feedback is gathered, analysed and actioned, as required. The documentation should also include the actions which need to be taken if the competent authority (in the UK this is the Medicines and Healthcare Products Regulatory Agency (MHRA)) requires to be contacted regarding a serious incident occurring with these 'in-house' devices.

The above documentation should be sufficient to enable a competent authority, or external auditor, to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and be sufficiently detailed to enable the competent authority to ascertain whether or not the general safety and performance requirements have been met, and the device is fit and safe for use.

The final requirement is that a public record of work carried out under these exemptions will be maintained. The record is to include, for each device manufactured or device modified, the contact details of the health institution and where the work was undertaken, how each manufactured or modified devices is identified – i.e. serial number, lot number, Unique Device Identification (UDI), identifier, general device description or, if required, a photograph of the device. These publicly available records may be accessible via the health care institution web site, the university web site, local library or other such easily accessible repository.

Further conditions are that the health institution must have the required resources, controls and finance available to ensure that the devices are manufactured as detailed in the documentation noted above.

4.4.2 M&H documentation to meet the exemption requirements.

Within the M&H quality system the following documentation cover the work to meet the above requirements.

- Document QP.02, ‘Project and Product Realisation’, details the control and documentation to the design, development and manufacture of items or devices including non CE marked medical or in vitro diagnostic devices, products or services for ‘in-house’ use only.
- Document QP.03F ‘Requirements for Product Realisation’ details the controls for the design, development and manufacture of CE marked medical or in vitro diagnostic devices, products or services.
- Document QP.03G ‘Academics and third Party Guidelines’ are guidelines for those working in collaboration with M&H on non CE marked medical or in vitro diagnostic devices, products or services for ‘in-house’ use only

4.5 The General Safety and Performance Requirements

The General Safety and Performance Requirements (GSPRs) are detailed as follows:

1. For Medical Devices

    a. In Annex 1 of the MDR

    b. In Schedule 3 parts 1, 2 and 3 of UK Legislation 2019 No. 791 Exiting The European Union, Consumer Protection, The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019, referenced as UK Legislation.

2. For In Vitro Diagnostic devices

    a. Annex 1 of the IVDR,

    b. In Schedule 17 parts 1, 2 and 3 of UK Legislation 2019 No. 791 Exiting The European Union, Consumer Protection, The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019, referenced as UK Legislation.

4.5.1 Comparison of EU and UK General Safety and Performance Requirements

A side by side comparison was undertaken to determine if the EU and UK GSPRs are, in fact the same, or similar, as had been alluded to by the UK Medicine Agency, when the noted that UK legislation '*….will mirror all the key elements contained……*' in EU legislation[(110)].

As can be seen from the two comparisons given in appendix C4 3 and C4 4, the current EU and UK legislation contains the same General Safety and Performance Requirements. The differences between the UK and EU GSPRs is detailed in tables 4.1 and 4.2, and are due to the UK legislation referencing, were possible, UK bodies or UK legislation.

This side by side comparison was also undertaken to ensure that the two M&H WIs[(102)], regarding the GSPRs for medical devices and in vitro diagnostic devices, contained all the required elements of both EU and UK legislation. In the future, the two side by side comparisons will be useful tools in reviewing new, or amended legislation, relating to medical and in vitro diagnostic devices. The side by side

comparisons are given in appendix C4 3 for Medical Devices and appendix C4 4 for In Vitro Diagnostic Devices.

The two comparisons show that there are no current ‘real’ differences between the EU and UK legislation.

To ensure that all of these safety requirements are met during the design and development of a medical device, two work instructions have been produced. These include a matrix showing all the GSPRs, if these are applicable. If they are applicable, the matrix shows which standards or recognised guidelines have been used to meet the GSPRs and where the GSPRs have been met, it states the evidence/documentation showing how the particular requirement has been met.

A sample of a blank matrix is given in Table 4.3.

The actual matrix for each type of device is given in WI-RD11 for Medical Devices and WI-RD10 for In Vitro Diagnostic Devices. Both documents form part of the M&H quality system.

Table 4.1 Differences in the Medical Devices EU and UK General Safety and Performance Requirements.

EU Legislation	UK legislation	Comment
10.4.1. Design and manufacture of devices	Design and manufacture of devices	
Devices, or those parts thereof or those materials used therein that: are invasive and come into direct contact with the human body, (re)administer medicines, body liquids or other substances, including gases, to/from the body, or	(7) Devices, parts of those devices or materials used in those devices listed in sub- paragraph (8) 8) The devices (or parts or materials) to which sub-paragraph (7) relates are devices which— (a) are invasive and come into direct contact with the human body; (b) administer or re-administer medicines, body liquids or other substances, including gases, to the body; or	In UK legislation the list of devices or types is given in Section (8) and not Section (7) While in the EU legislation these are listed in 10.4.1. When taken as a whole, the two sets of requirements for design and manufacture of devices are the same.

transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body,	(c) transport or store medicines, body fluids or substances, including gases, to be administered or re-administered to the body	
10.4.Substances 10.4.1. (a), (b)	Substances 10 - (7) (a), (b)	The UK legislation gives more exact details as to the legislation and which parts are applicable.
10.4.2. Justification regarding the presence of CMR and/or endocrine-disrupting substances 10.4.3 Guidelines on phthalates 10.4.4 Guidelines on other CMR and endocrine-disrupting substances	10 - (9)The justification for the presence of the substances listed in sub-paragraph (7) must be based upon—	The wording in these paragraphs differs but the meaning and the end requirements are the same. when either EU or UK legislation is updated or amended these this requirement must be reviewed for any differences in requirements
Devices incorporating materials of biological origin 13.1	Devices incorporating materials of biological origin 13 - (1)	The EU requirement points to EU legislation while UK legislation point to UK legislation. These may differ in the future. The two sets of legislation need to be reviewed in the future for differences.

Devices incorporating materials of biological origin 13.2	Devices incorporating materials of biological origin 13 – (2)	The wording is different but the meaning is the same.
Construction of devices and interaction with their environment 14.7	Construction of devices and interaction with their environment 14 – (7)	The wording is different but the meaning is the same. To ensure safe disposal of devices and any resulting waste products or sundries.
Devices with a diagnostic or measuring function 15.2.	Devices with a diagnostic or measuring function 15 (2)	These two paragraph point to different legislation. Just now the legislation is the same but it may vary in the future.
16.2.Intended radiation	*Point* 16 (3)	Words differ but their meaning and the requirements are the same.
Label and instructions for use 23.1 Points (f) and (h)	Label and instructions for use 23 (1) Points (f) and (h)	The two requirements are the same but may vary in the future as the EU legislation alludes to future changes or work in other areas.

Table 4.2 Differences in the In Vitro Diagnostic Devices EU and UK General Safety and Performance Requirements.

EU Legislation	UK legislation	Comment
Chemical, physical and biological properties 10.2.	Chemical, physical and biological properties 10 – (2)	Not the same wording but the same meaning and requirement.
Information on the label	Information on the label 20 – (3)	Note how the UK legislation does not look outside of UK – for example see para (3) (p) of schedule 17 UK legislation versus section 20.2 (p) of Annex 1 of the IVDR.
Information in the instructions for use 20.4.1	Information in the instructions for use 20 – (7)	EU legislation paragraphs 20.4.1 (ag) and (ah) are noted in UK legislation point 20 – 7 (a) and 20 – 7 (b)

Table 4.3 Extract from a General Safety and Performance Requirements Matrix

Essential Requirement 11 Infection and microbial contamination	A NA	Standard	Supporting Documentation	Location of supporting documentation
11.1. Devices and their manufacturing processes shall be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the user or, where applicable, other persons. The design shall: (a) allow easy and safe handling; (b) reduce as far as possible any microbial leakage from the device and/or microbial exposure during use; and, where necessary (c) prevent microbial contamination of the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen.				
11.2. Devices labeled either as sterile or as having a specific microbial state shall be designed, manufactured and packaged to ensure that their sterile condition or microbial state is maintained under the transport and storage conditions specified by the manufacturer until that packaging is opened				

at the point of use, unless the packaging which maintains their sterile condition or microbial state is damaged.				
11.3. Devices labeled as sterile shall be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.				

4.6 Technical File documentation

Medical or in vitro diagnostic device manufacturers (or others placing devices on the market) have various options for having their devices assessed against the relevant regulations. These options vary, from having each device, or batch of devices, tested by a notified body to the notified body auditing both the quality management system and the technical file for device in question. (See Tables 4.4 and 4.5 and Figures 4.1 and 4.2 for the various assessment routes for both medical and in vitro diagnostics devices.)

The compliance route which M&H have chosen for medical and in vitro diagnostic device assessment is by the conformity assessment of the M&H QMS and the device technical file. The conformity assessment is an audit by a notified body. The requirements for this type of assessment under the UK law, are detailed in Schedule 10 for medical devices and Schedule 24 for in vitro diagnostic devices, whereas, for EU legislation, these are detailed in Annex IX of the MDR and the IVDR. (Note at the time of writing this thesis the introduction of the MDR was delayed by 12 months. Hence the MDD is still the legislation in force and to be followed.)

The technical file requirements for in vitro devices are detailed in Schedule 18 of the UK law and Annex II of the IVDR. These requirements for medical devices are detailed in Schedule 4 of the UK law and Annex II of the MDR.

These documentation requirements relate to the device, device variants and associated accessories.

Each device should also have a design history file or evidence as to how the design evolved and that the design was developed in accordance with the approved design plan and changes were reviewed and approved. This history file must be maintained until at least the end of life of the last device manufactured and preferably within the device's technical file.

The requirements contained in these Annexes and Schedules are there to ensure that the developed device and its associated documentation have been designed, tested and reviewed to verify that the use of the device outweighs any residual risk or hazards still associated with the device. Also required are details of how post market surveillance control and management is achieved and finally, that a Certificate of

Conformity to the relevant legislation is produced and signed by an appropriate senior member of staff.

It is essential to ensure that the product meets all the legislative requirements and passes any audit undertaken of the device by the notified body.

It should be noted that in the M&H QA system the technical documentation requirements and the post market surveillance requirements are detailed in one document. How post market surveillance is undertaken, controlled and as required reported to the relevant authorities is described in section 4.7 of this thesis '*Post market surveillance and Vigilance.'*

Annex C4 5 is a comparison of the requirements for technical file documentation given in the EU regulations with those given in the UK Law. The comparison shows no substantive differences between the two.

4.6.1 Summary of In Vitro Diagnostic Device Technical Documentation

1. Certificate of Conformity as detailed in Annex IV of the IVDR[(3)] or Schedule 20 Regulation 1A of UK law[(4)].
2. Device Description, Variants, Accessories and Specification
3. This section will describe the device in terms of function and use, any accessories included, and variants planned, plus, as a minimum, the following;
    - 3.1 UDI information as per IVDR Annex VI Part C or UK legislation Part C of Schedule 22.
    - 3.2 what the device is supposed to detect, or measure.
    - 3.3 is the device automated and how is this automation controlled.
    - 3.4 the risk classification of the device as per IVDR Annex VIII
    - 3.5 the intended users and the target patient population
    - 3.6 references to previous or similar devices.
4. Information supplied by the Manufacturer will include a copy of the instructions for use and copies of all the labels placed on the device or the device packaging. Note that marketing materials should also be under document and change control. This will ensure such document is correctly

controlled and changes to marketing materials do not lead to errors in device claims or uses in marketing materials.

5. The Design and Manufacturing Information required is as follows:
   5.1 A full understanding of how the design and development of the device was achieved from specification to design sign off.
   5.2 Full details of the manufacturing process and how devices are tested prior to release to customers/users. The information must include a list of where assemblies or sub-assemblies are sourced and the location of offsite manufacturing and subcontractors.
6. General Safety and Performance Requirements.

   This information will be contained in the matrix given in WI-RD.10 - IVDR General Safety and Performance Requirements Matrix(102) once it has been completed.

7. Risk/Benefit Analysis and Risk Management.

   This section will contain the rationale and results of the risk assessment (carried out according to WI-RD-05(102) and will include a summary indicating why any residual risks are outweighed by the benefits obtained from the device. See also EU Annex Section 1, 3 and 8, and UK Schedule 17, paragraph 1, 3 and 8

8. Product Verification and Validation

   The documentation shall contain the results and critical analyses of all verifications and validation tests and/or studies undertaken to demonstrate conformity of the device with the requirements of the relevant legislation.

9. Device Performance

   The documentation should state the type of sample to be used by the device and how this sample is to be obtained, including the volume or size of the sample. The documentation should also detail any sample preparation prior to being used in the device.

10. Device Accuracy.

The documentation must give details of the device accuracy, how this was determined and proved, how the devices is initially calibrated or checked and how the device is maintained during its use.

11. Clinical Performance and Clinical Evidence

The documentation needs to detail the method and results of both laboratory and clinical testing to determine the device performance or evaluation of the device in use. Also, any trials carried out shall be summarised in this section along with the location of the reports resulting from these trials. Any documentation, which would preclude clinical trials from being carried out, should be detailed in this section. When required the report detailed in Annex XIII must be produced.

12. Stability

The documentation must outline the methods and the results of testing the device's lifetime, in use, transport and storage stability.

13. Software Validation and Verification

The documentation should contain details of the rationale and the results of validation and verification of the software included with the device, and any device variants. The details should also outline the software/firmware included in the device, or any application software to enable the device to interface to external devices, user interfaces or accessories.

14. Additional Information

For specific types of devices, it may be necessary to provide additional information in the documentation to ensure that the device is correctly designed, developed and manufactured. These devices include:

14.1 Sterile devices – how sterilised and how sterility is maintained during transport and use. Note any sterilisation process used must be documented and validated.

14.2 Devices with a defined microbiological element, details of the sterilisation process or how they will be sterilised should be included in

the documentation. Also, instructions should be given for products to be sterilised by the user prior to application, where appropriate.

15. Quality System

In the documentation, this section should describe the quality system controlling the design, manufacture and inspection of the device and specifying any documentation of particular relevance. If subcontractors are involved, details of their quality systems shall be included. This section may state a list of relevant standards to which the manufacturer, and any subcontractors or third parties, are accredited.

16. Standards

The documentation in this section should list the standards followed or referred to within the technical file. These shall be mentioned throughout the technical file where applicable, particularly in the Essential Requirements Matrix. Using a harmonised standard give a presumption of conformity if applied in the appropriate manner. A current list of the harmonised standards can be found at the relevant EU website. Non-harmonised standards may also be used.

17. Self-testing Devices

Class B, C and D devices for self-testing or near-patient testing the requirements for technical documentation assessment set out in Section 5.1 of Annex IX will need to be met.

18. Changes and additions

All changes to the design or manufacture of the device shall be incorporated into the technical file, as required. Changes to product or devices placed on the market are initially documented on action forms. Copies of these forms will be kept in this section of the technical file.

19. Post Market Surveillance Plan

This documentation shall detail how the performance of the device in use is to be monitored; How the customer feedback is to be analysed; How knowledge of the device failings will be conveyed to any users of the device and relevant authorities; The plan needs to be reviewed against Annex III and

Annex XIV and Schedule 14 and 19 and or definitions given in the legislation. For example

19.1 UK Law paragraph 121.Post-market surveillance system of the manufacturer, or

19.2 EU Legislation, IVDR, Article 78 Chapter VII Post Market Surveillance, Vigilance and Market Surveillance.

4.6.2 Summary of Medical Device Technical Documentation

1. A Certificate of Conformity as detailed in Annex IV of the MDR or Schedule 6 Regulation 1A of the UK legislation.

2. Device Description and Specification

   2.1 A technical description of the device, its operation and details of any novel features.

   2.2 An outline of the clinical need for the device, the indicated patient population and any contraindication to it's use.

   2.3 The risk classification as per Annex VIII MDR or Schedule 9 of UK law.

   2.4 A description of the physical device - including size, weight and performance characteristics.

   2.5 Details of all the materials used, especially those contacting the patient. Where required, information relating to previous version(s) of the device or similar devices on the market.

   2.6 The UDI information as required by Part C of Annex VI or Schedule 8 of UK law.

3. Information Supplied to the User

   The documentation must state all the information supplied to the user, not just the user instructions but the labelling information on the packaging or the device, the transport packaging and multipacks etc. This information must also be in the languages of the countries or areas to which the device will be supplied. Note that marketing materials should also be under document and change control. This will ensure such document is correctly controlled and changes to marketing materials do not lead to errors in device claims or uses in marketing materials.

4. Design and Manufacturing Details

   4.1 The documentation must give full details of all the design stages of the device. The detail of this section has to be sufficient to enable a full understanding of the device development, from its concept and specification to manufacture and completion.

4.2 There needs to be a comprehensive narration of the assembly and manufacturing instructions including the manufacturing test and calibration details.

4.3 Validation and verification of the manufacturing processes must be fully stated.

4.4 All information relating to manufacturing sites and third parties used in either the design, assembly or manufacture of the device must be given.

5. General Safety and Performance Details

The information required must be able to demonstrate compliance with Annex 1 of the MDR or schedule 3 of the UK law. In most cases this will be the completed essential requirements matrix and supporting documentation, See WI-RD.11, MDR General Safety and Performance Requirements(102).

6. Risk Analysis and Management of Risk.

The documentation should contain details of all risks foreseen or discovered during the development of the device; an analysis of these risks and how they were managed to reduce them to a low as level a possible; a statement as to why any residual risks are tolerated and how the benefit of the use of the device outweighs these risks.

7. Product Testing

The documentation shall contain details of the testing carried out to ensure that the product has:

7.1 Achieved the specified technical requirements - verification,

7.2 Met the requirements of the customer and that the device is fit for purpose – validation testing.

The details of how the testing was carried out and the test results should also be included. Information should disclose how any test failures were reviewed and if any testing resulted in design changes.

The testing may include pre-clinical or clinical testing and animal testing, laboratory testing or device hardware or software simulation. All ethics

approval whether NHS, academic or regulatory body, must be referenced. See also Annex XIV of the MDR and Schedule 14 of the UK law.

8. Additional Details

Specific details are required for:

8.1 Devices which incorporate a functioning medicinal produce

8.2 Devices incorporating a tissues or cells.

8.3 Devices which deliver substances into the human body.

8.4 Devices delivered sterile or predefined microbial state.

9. Matrix of General Safety and Performance Requirements

The documentation should contain a matrix detailing each GSPR, any applicable standard, a statement of how the requirement has been addressed and where the relevant documentation can be found. This matrix can be found in WI-RD.11, MDR General Safety and Performance Requirements'[(102)].

10. Quality System

This section should describe the quality system controlling the design, the manufacture and inspection of the device and any documentation of particular relevance. If subcontractors are involved, details of their quality systems shall be included. This section may be a list of relevant standards to which the manufacturer and any subcontractors or third parties are accredited to.

11. Standards

This section lists the standards followed or referred to within the technical file. These shall be mentioned throughout the technical file where applicable, particularly in the Essential Requirements Matrix. Using a harmonised standard give a presumption of conformity if applied in the appropriate manner. A current list of the harmonised standards can be found at the relevant EU website. Non-harmonised standards may also be used.

12. Class I Devices

The requirements for Class I devices are controlled by WI-RD.04. The technical file containing copies of documentation generated under this section to contain the words 'Self Declaration' in its title.

13. Changes and additions

All changes to the design or manufacture of the device shall be incorporated into the technical file as required. Changes to the product or devices placed on the market are initially documented on action forms. Copies of these forms will be kept in this section of the technical file.

14. Post Market Surveillance Plan

At this part, the documentation shall narrate; How the performance of the device in use is to be monitored; How the customer feedback is to be analysed; How information regarding device failings will be conveyed to the users and relevant authorities; The post market surveillance plan must meet the requirements of the relevant legislation – Annex III and Annex XIV, MDR, or Schedule 5 and 14 of the UK law plus the supporting articles or definitions given in the legislation. For example:

14.1 UK Legislation paragraph 121.Post-market surveillance system of the manufacturer, or

14.2 EU MDR Legislation Article 83, Chapter VII Post Market Surveillance, Vigilance and Market Surveillance.

4.7 Post Market Surveillance and Vigilance.

Due to the scandals surrounding defective devices[111,112], the severity of device faults being under estimated, faulty devices not being rectified or removed from the market and notified audit bodies not picking up on serious issues with devices, the requirements to relating to post market surveillance have been significantly tightened.

Post market surveillance is used to determine how a device operates after it has been put into service or use. The surveillance includes reviewing the processes used during the manufacturing, marketing and shipping phases and not just problems found once the device has been put into use.

Vigilance is used to ensure that any reports of defective devices, similar devices, materials or device operation are reviewed and acted upon by the appropriate competent authorities. This action may range from issuing a note to user to inform them of the possible problem and to change the method of use through to a full product recall. The action may also require the manufacturer to inform the relevant competent authority and have the problem entered in the relevant device database e.g. EUDAMED – See section 4.10 '*Unique* Device Identification System' below**.**

The data gathered from post market surveillance activities is used to trigger vigilance activities[113].

4.7.1 Comparison of EU and UK requirements for Post market surveillance and Vigilance activities.

A comparison between the EU regulations and the UK legislation was undertaken to compare the new legislation; MDR to IVDR and then EU against UK legislation. The comparison highlighted the areas where medical device requirements varied from in vitro diagnostic device requirements. The variations were due to the differences between types of devices and the information required to ensure these devices remained safe and fit for use.

One of the major differences is the Post-market Performance Follow up plan (PMPF) for in vitro diagnostics devices, while for medical devices, there is a Post-market Clinical Follow up plan (PMCF), is required[114]. (See section 4.7.4 for outline of PMPF and PMCF).

One outcome from these comparisons has been to identify the areas which are similar and allow these areas to be consolidated into one quality control document. The areas specific to either medical devices or to in vitro diagnostic devices can then be placed into separate control documentation and appropriately applied to the intended device.

Post market surveillance is also to be carried out on devices manufactured solely for ‘in-house’ use. This is a new requirement introduced in both EU and UK legislation and is to ensure that any device, manufactured ‘in-house’, is fully monitored, and problems reported are reviewed and acted upon, even to reporting the problem to the appropriate regulatory authority.

4.7.2 Post Market Surveillance Summary

As stated above, post market surveillance has a common set of requirements for both in vitro diagnostic devices and medical devices, and a specific set of requirements covering the differences in both types of devices.

4.7.3 Activities to be undertaken and data to be collected

A fully documented post market surveillance system, when implemented, ensures that the required surveillance and vigilance activities are carried out and controlled. Any data, gathered from these activities, should be appropriately analysed and the findings reported or published to those concerned, including competent authorities, notified bodies, and device users.

This system of post market surveillance will ensure that the data gathered is used as follows:

1. To update the risk and hazard analysis so as to ensure that the risk-benefit derived for the device is still valid.
2. To identify the necessary corrective action e.g.
    a) update the user instruction or labelling requirements.
    b) review and update the manufacturing and design information for the device.
    c) review and update either the medical device clinical performance or the in vitro diagnostic device evaluation data.

3. Ensure that reports and corrective actions, including device safety notices or recalls, are intimated within the specified time scales and to the appropriate authorities or persons.
4. Ensure the PMCF plan for medical devices or PMPF plan for in vitro diagnostics devices is produced and issued. (It is to be noted, that justification as to why a PMCF/PMPF is not applicable must be issued).
5. Production of a Periodic Safety Update Report (PSUR). See section 4.7.4 for outline of PSUR).

The activities related to the requirements of the post market surveillance system will need to be defined. These activities[113, 114, 115, 116, 117] include:

1. the processes to be used to collect and methods used to analyse the data required to meet the requirements detailed in Article 83 of the MDR or IVDR and UK legislation para 121 and para 186),
2. the indicators and thresholds to be used in reassessing the benefit risk,
3. how complaints and other feedback will be investigated and assessed,
4. the processes to be used to identify trends and determine if these are reportable,
5. how to identify and initiate corrective actions,
6. how vigilance information and other information (PSUR, PMPF and PMCF) are to be produced, reported and the time scales to be met in producing and issuing these report, and
7. the methods used to identify devices involved in corrective actions and how to trace these devices if required.
8. the output of post market surveillance activities, including PMPF, PMCF and PSUR will be regularly reviewed. Within the M&H QA system this review is undertaken during the M&H quality system management reviews.

4.7.4 Post Market Clinical Follow-Up, PMCF, Post Market Performance Follow-Up, PMPF and Production of a Periodic Safety Update Report, PSUR overview

The following are short overviews of PMPF, PMCF and PSUR.

4.7.4.1 Post Market Clinical Follow-Up, PMCF

During the design and development of a medical device, the clinical performance of the device must be reviewed and tested to ensure it meets the both the customer requirements and design specification. The PMCF is a continuation of this process. The PMCF updates the clinical evaluation by assessment and analysis of clinical data or reports obtained from the operation of the device will in use to ensure the clinical safety and performance of the device when used as intended by the manufacturer.

4.7.4.2 Post Market Performance Follow-Up, PMPF

During the development of an in vitro diagnostic device the performance of the device must be tested to ensure it meets the required performance level. This performance evaluation must show the scientific validity of the device and proof that the device meets the required analytical and clinical performance. The performance evaluation must be such that it shows the device achieves the intended clinical benefit and safety, when used as intended by the manufacturer. PMPF is the ongoing evaluation of the devices scientific validity and ensuring that the devices continues to meet the intended analytical and clinical performance.

4.7.4.3 Periodic Safety Update Report, PSUR

The PSUR is a report, to be produced on a yearly basis for the lifetime of moderate to high risk medical or in vitro diagnostic devices. For each device, report should contain for example the main findings of the PMCF and PMPF, the conclusions from updated benefit-risk determination, the number of devices sold, analysis of the device users and if possible actual device usage.

4.7.5 Post Market Surveillance System to meet the exemptions required for 'in-house' designed and manufactured devices.

The exemptions for 'in-house' manufacture detail that 'the health institution reviews experience gained from the clinical use of the devices and takes all necessary corrective actions.'(4) Hence, some form of post market surveillance is required, especially as the exemption required by the General Safety and Performance Requirements and these requirements include the need to evaluate and analyse the impact of information from reports from:

1. the manufacture or production of the devices and the information relating to the device and
2. the post market surveillance related to the device once it had left the manufacturing or production area.

The evaluation of this information is continuous. The evaluation needs to provide details on the hazards reported, their frequency of occurrence and an estimate of their associated risks. The result of the evaluations should indicate the overall risk of continued use of the device and if this risk is acceptable.

The post market surveillance will also need to fulfil the requirements of the quality system implemented by the health care institution to control 'in-house' manufacture and work undertaken in collaboration with academics and third parties. These requirements will need to be equivalent to those detailed in both BS EN ISO 13485:2016 and BS EN ISO 15189:2012 related to post market surveillance.

Accordingly, the health care institution will need to implement a system to meet the post market surveillance requirements of the exemption.

4.8 Risk management and Hazard reduction

This area of the EU regulations and UK law in relation to medical devices and in vitro diagnostic devices is asking that during the development of the device all foreseeable hazards, posed by the use of the device, are reviewed to determine the risk they might pose to the user, the patient or others. At the end of the development, there needs to be a determination made that the device is safe to use and the risks, posed by any residual hazards, are outweighed by the benefit of using the device. A declaration to this effect needs to be made and formally noted in the technical file.

The first area of risk management is to determine the risk classification of the device which determines the perceived risk in relation to the EU and UK legislation. The classification rules are detailed in the section 4.9 '*Device Classification Rules'***.** The scrutiny given by the notified body and the relevant competent authority, during the review of the device and the results of post market surveillance analysis, will depend on the outcome of this determination. The scrutiny can vary from the actual device being tested and reviewed by an expert panel to a review of the technical file, or indeed, the self-declaration that the device meets the requirements. Figures 4.1 and 4.2 outlines the assessment routes dependant on the risk classification of the device.

The second area of risk management is to undertake continuous reviews to determine the risk or hazards posed by the transport, the manufacture and the actual device in use.

All risk management and hazard identification should be undertaken according to the relevant issue of standard ISO 14971[(169)] '*Risk management for medical devices*' and following the guidance given in ISO/PRF TR 24971:2020[(168)] '*Medical devices — Guidance on the application of ISO 14971*'. In the EU and UK legislation at the section entitled '*General obligations of manufacturers*', point 2, requires that manufacturers '*document, implement and maintain a system for risk management'*.

The comparisons given in appendix C4 6 show that the requirements of all three sets of legislation are similar and the only notable differences are:

- different authorities to report to
- variation in legislative references and
- no requirement for in vitro diagnostic devices relating to the reprocessing of single use devices.

The EU and UK legislation require that a risk management system is established, adhered to and audited by notified bodies – external auditors.

In summary the risk management system must determine the known or possible risks and hazards associated with a device and evaluate these risks and hazards to determine their severity and likelihood of occurrence. Unlike the previous directives – IMDD, MDD and IVDD, the MDR and IVDR require that risk are reduced to a low a level as possible. Hence , an action plan to reduce these risk or hazards to a low as level possible must be produced, and the risks and hazards re-evaluated, once the plan has been actioned.

This risk management process is only completed once the risks and hazards identified, are deemed to be acceptable. That is, the benefit gained from using the device, whether a medical device or an in vitro diagnostic device, outweighs the risk or hazard associated with using the device.

Risk management is not about the device itself but needs to examine the device and possible misuse or other uses of the device, for example, the expected environment that the device will be used in, who the users of the device are and the intended patient group.

Typical risk and hazard reduction methods include having appropriate alarm sounds and indicators, user instructions detailing how to use the device and the safety warnings and contra indications to use. User training can also be used to reduce any residual risks or hazards associated with the device. The sale of the device may also be restricted to ensure only trained or those with appropriate qualifications are provided with the device. All identified risk and hazards must be reduced to a low as level as possible. Only if the final level of risk or hazard is acceptable, should the device be placed on the market or into use.

Risk management also extends to how the device is packaged and transported to ensure it reaches the customer in the proper condition for use. Hence, the transport and storage conditions need to be evaluated to ensure that these do not cause the device to become hazardous. It should be noted that devices need to be evaluated specifically for risks and hazards associated due to their use if they are portable, wheeled or with use with ambulatory patients.

The risk management system must also ensure that any feedback relating to the device, whether from the manufacturing phase or the in service phase (for example from users, patients and sales staff), is reviewed to determine if this feedback requires re-evaluation of the risk and hazard of the device.

Accordingly the post market surveillance system must have a link into the risk management system.

Risk management is a continuous process for the life time of the device from pre design phase to user phase to disposal or scrappage. All new risks or hazards identified during the lifetime of the device from design, development and testing phases are documented, analysed and reduced.

Devices manufactured for ‘in-house’ use only will also be required, without exception, to meet these same risk management controls.

A new M&H work instruction detailing the risk management system used within the M&H quality system is to be produced.

4.9 Device Classification Rules.

These rules define the level of risk associated with the use of a particular device or family of devices. The risk classification of the device determines the possible conformity assessment routes for a device. The higher the risk classification, the stricter, and more onerous, the conformity assessment examination procedures will be.

In order to determine the risk class of a device, it is necessary to first determine the nature or type of the device and then work through the appropriate classification rules in order.

A comparison of the rules for the UK and EU In Vitro Diagnostic Device legislation given in Appendix C4 7 and Medical Devices Appendix C4 8, indicates that, in essence, they are the same.

The classification rules to be followed during a development will depend on which market the device is intended for.

4.9.1 Classification rules for 'In-House' devices

For all cases/types of devices, items, accessories or modifications developed and manufactured for 'in-house' use (NHS Tayside) the UK classification rules will be reviewed.

4.9.2 Classification rules for CE marked device

The rules that require to be followed will depend on the eventual geographical market that the device is to be sold into. If in the EU only, then the EU classification rules apply, and if in the UK only, then the UK classification rules are applicable. If both EU and UK areas are the intended destinations then both sets of classification rules need to be invoked.

For the time being following EU or UK classification rules should lead to the same device risk classification.

4.9.3 Classification Rules for Software

These rules also apply to the software used in medical or in vitro diagnostic devices or where the software is used as the device.

4.9.4 Background to the changes in Device Classification Rules

The classification rules for both medical and in vitro diagnostic devices have been updated to bring them into line with the International Medical Device Regulators Forum, (which superseded the Global Harmonization Task Force[184]) guidelines.

The changes in the device classification rules are most noticeable in the In Vitro Diagnostic Devices Regulations.

The guidelines for in vitro diagnostic devices have also been driven by changes in the technology used in vitro diagnostic device, the need to correctly assign risk level to new types of in vitro diagnostic devices and to standardise device risk levels across the globe.

When the original In Vitro Diagnostic Device Directive was introduced, many of the in vitro diagnostic devices which are in use today were not envisaged – for example genetic tests. At one time, these were only available via a specialist laboratory, but they are now readily available over the counter. Similarly, fertility testing and now the field of companion testing – where one test is to determine if a condition exists and a follow on test is to determine the response to the condition of a single or multiple drugs. Previously, they were not available as products[118]. Further examples are wearable biosensors, which are coming to the market and which will eventually bring predictive diagnosis to the user via a smart phone or similar device.

The new in vitro diagnostic device classification has been extended to 4 classes of device risk whereas the old IVDD had only two classes of risk – Self Certification and Notified Body assessment as detailed in the two lists given in Annex II of the IVDD directive[10].

A point to note is that these changes in the in vitro diagnostic device classification rules will result in 80% of IVD being reviewed by a notified body in comparison to only 20% being reviewed under the old IVDD classification rules [120]. This increase in notified body work load, coupled with a large reduction in notified bodies looking

to be re-designed to the IVDR, is likely to cause problems in finding a notified body who can allocate time to asses a new device[120,121].

4.9.5 In Vitro Diagnostic Devices classification rules – overview

The IVDR classification rules are contained in Annex VIII of the IVDR and Schedule 23 of the UK MDR legislation.

Both EU and UK classification rules are separated into Implementation Rules and Classification Rules.

The Implementation Rules detail how the classification rules have to be applied and how to apply the rules for different scenarios or application. These rules also apply to software used in the devices or as a device.

There are 7 Classification rules to be applied in the classification of IVDDs and there are currently 4 classes of devices (A, B, C and D). Class D being the classification of highest risk i.e. devices where an incorrect test poses a serious threat to life. Class A devices are the lowest risk devices; these include specimen holders, buffer solutions and washing solutions.

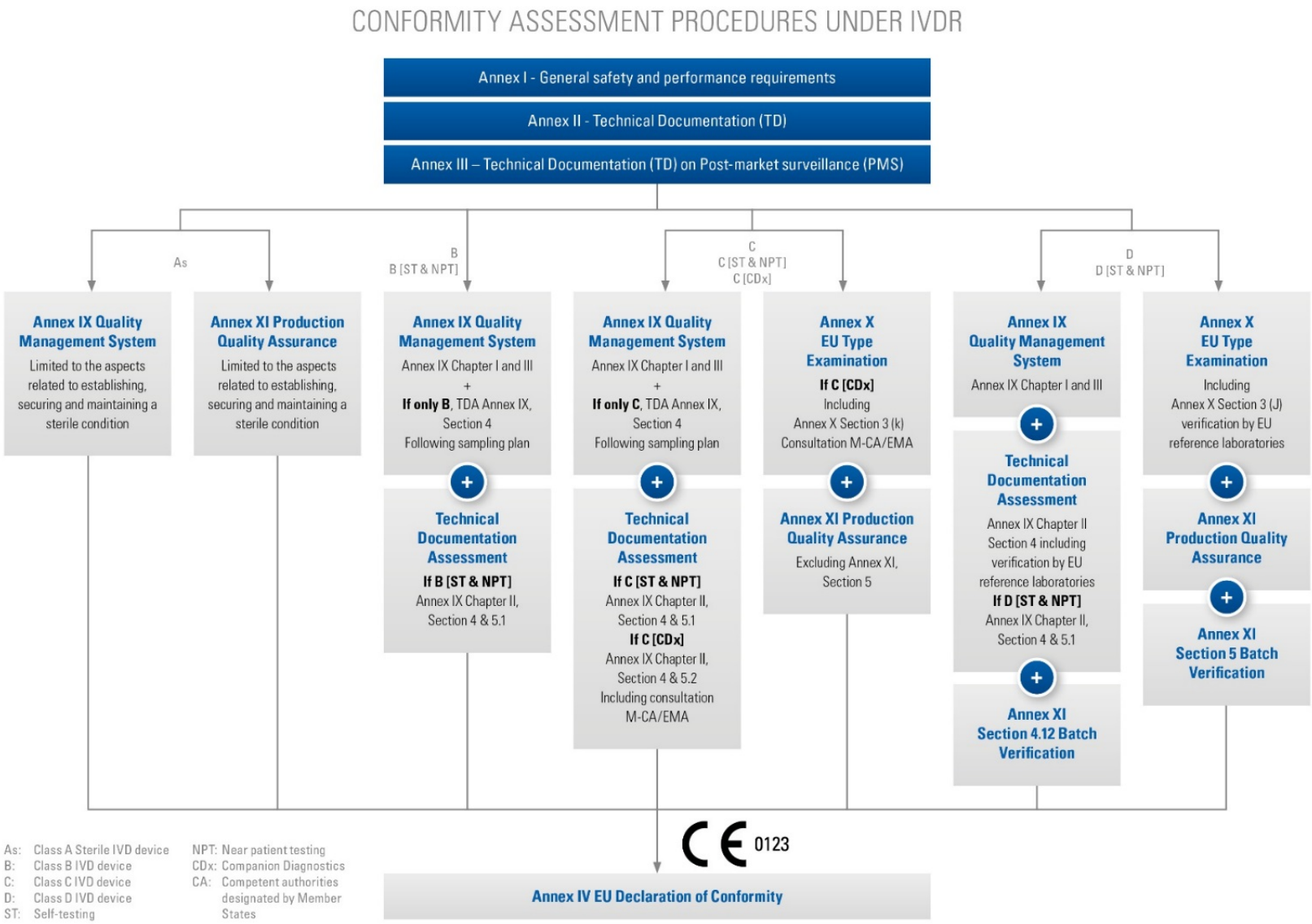
4.9.6 In Vitro Diagnostic Device Classification and route to certification

Table 4.4 and Figure 4.1, noted below, gives an overview of the routes to assessment and certification for In Vitro Diagnostic Devices[122,123,124,125]. As can be seen these routes are heavily dependent on the device risk classification, and hence the importance of correctly classifying the device. External auditors will challenge the risk classification of a device and may request that the classification be reviewed by a third party,

Table 4.4 An overview of assessment and certification routes for In Vitro Diagnostic Devices[122,123,124,125]

Class A	No external review or supervision - have an appropriate QA system and documentation as required	Low personal risk Low risk to public health
Class B	External body review - assessment of QA system.	Moderate individual risk Low risk to public health
Class C	External Body review, full assessment of technical documentation. Production of periodic safety update.	High individual risk Moderate risk to public health
Class D	External body review, full assessment of technical documentation and as required review by specialist group and testing by a reference laboratory. Production of periodic safety update.	High individual risk High risk to public health.

Figure 4.1 Detailed conformity assessment for In Vitro Diagnostic Devices showing how the assessment routes vary with device risk classification[(125)]



4.9.7 Medical Devices Classification Rules - An Overview

The classification rules for medical devices are contained in Annex VIII of the MDR and Schedule 9 of the UK Law.

Similar to the Classification Rules for In Vitro diagnostic Devices, the EU and UK classification rules for Medical Devices are separated into Implementation Rules, Classification Rules, and a section giving definitions of terms used in these classification rules.

In comparison to the seven Classification rules for In Vitro Diagnostic Devices, there are twenty two Classification rules to be applied in the classification of medical devices and four classes of devices Class I, IIA IIB and III. Class III being the classification of highest risk e.g. devices where there is a fault in the device or in its manufacture and poses a serious threat to life. Class I devices are the lowest risk devices where the use of the devices or poses little or no risk of harm.

4.9.8 Medical Device Classification

The medical device classification requirements are now a combination of the rules relating to implantable and active medical devices directives. The EU MDR and UK law retains the same number of risk classes as the old MDD – that is four. The changes to classification rules for medical devices have taken into account devices which are absorbed into the body, devices which use biological product(s) to provide a therapeutic effect, and that the invasiveness into the body of a device. The risk classification rules include the risk posed by nano-materials and also software, as a standalone device. Changes to the rules, including the addition of device types to certain of these rules, will increase the number of devices placed in the Class III category[126,127,128]**.** For example, devices coming in to contact with the spinal cord are now class III.

4.9.8.1 Class I devices – and a new superset - Reprocessing

Normally class I devices are self-certificating devices, that is, the manufacturer declares that the device meets the requirements of the directive and places them onto the market without the need for an external scrutiny of the technical files. There is a superset of Class I devices where a particular part of the device's

technical file has to be reviewed. These are Class I devices with either a measuring function, or are to be delivered or are to be sterilised or are to be reprocessed. An external review of the measuring function, sterilisation or reprocessing instructions will be required by an appropriately registered notified body. Reprocessing is new to this Class I superset. The MDR now requires device manufacturers to produce validated instructions for the reprocessing of reusable devices[130]. Health Institutions also will have to abide by the Article 17 of the MDR and Schedule 16 of the UK legislation relating to reprocessing of medical devices[131, 194].

4.9.8.2 Devices with a non-medical purpose

Several devices without medical purposes are placed under the control of the MDR or UK legislation. Many of these devices are related to cosmetic uses, for example lasers for tattoo removal, contact lenses, devices for skin resurfacing and certain devices for modifying brain neuronal activity. Hence it is imperative to review the groups of products without an intended medical purpose to determine if they come under the remit of the MDR or the UK legislation. These non-medical products are detailed in MDR Annex XVI or Schedule 16 of the UK legislation.

4.9.9 Medical Device Classification conformity assessment routes

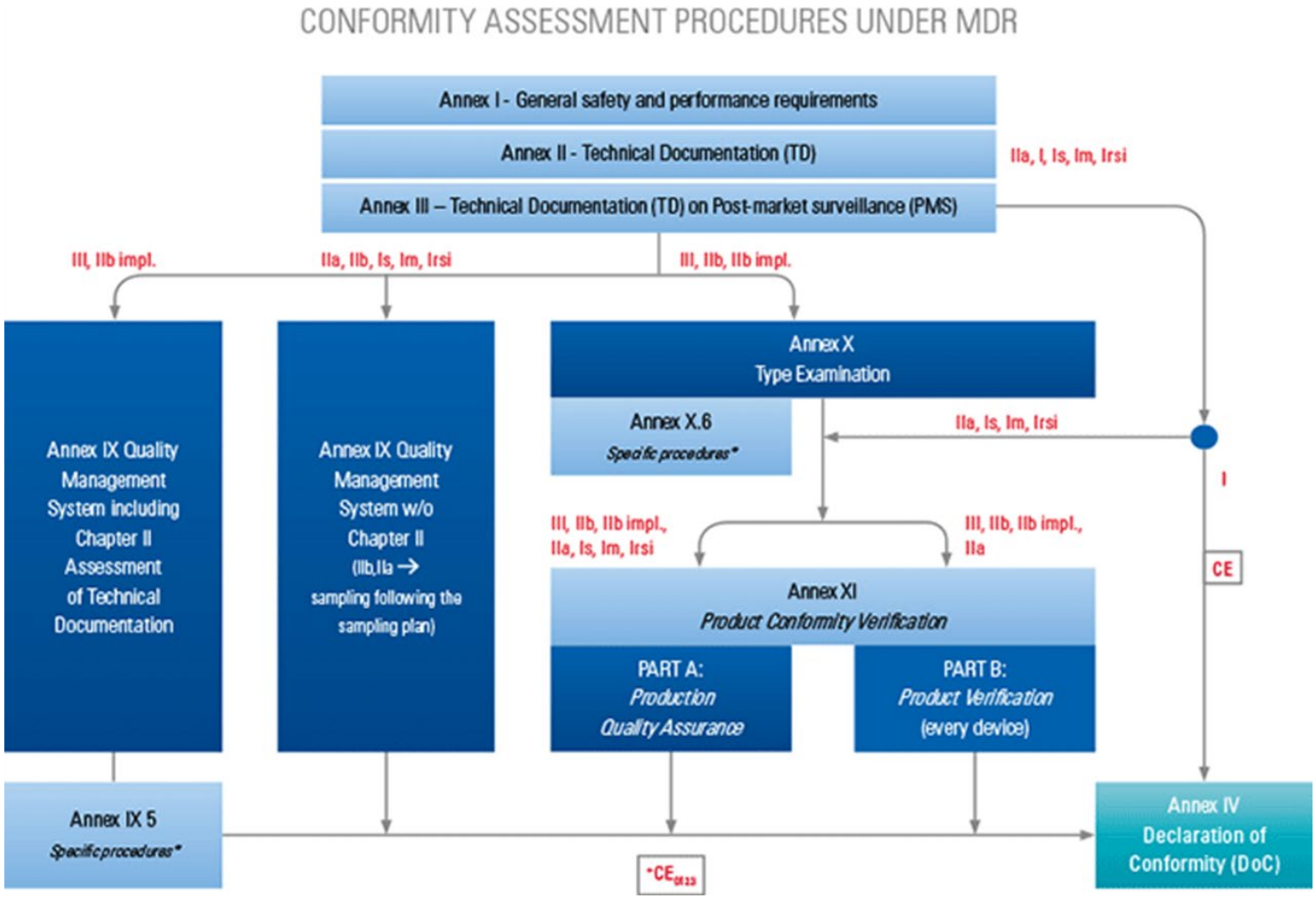
The routes to assessment and certification for a medical device, are like those for an in vitro diagnostic device, and are dependent on the risk classification of the device[128,132, 133]. Table 4.5 and Figure 4.2 gives an overview of these routes.

Table 4.5 An overview of assessment and certification routes for Medical Devices[128,132, 133].

Class I	No external supervision but have an appropriate quality system and technical documentation	Low individual risk Low risk to public health
Class I with S, M, R	Only the Sterility, measurement or reprocessing parts of the device technical file are reviewed by an external body	Low to Moderate personal risk Low risk to public health
Class IIA	Produce a periodic safety up date, have product assessment or technical file assessment as required.	Moderate individual risk Low risk to public health
Class IIB	Produce a periodic safety up date, assessment of technical files for all products to be placed on the market.	High individual risk Moderate risk to public health
Class III	Produce a periodic safety up date, assessment of technical files for all products to be placed on the market. Clinical evaluation reports and possible reporting to notified body of batch manufacture results.	High individual risk High risk to public health.

S- Sterility, M – Measurement, R- Reprocessing part or all of a surgically reusable instrument.

Figure 4.2 Detailed conformity assessment procedures for Medical Devices showing how the assessment routes vary with device risk classification[(128)]



4.10 Unique Device Identification System

The new medical device legislation introduces a system to enable identification of the device, whether a medical or an in vitro diagnostic device, to its point of origin. This unique identification is to ensure the control and ongoing safety of a medical device or an in vitro diagnostic device from the factory to the end user.

4.10.1 The need for the Unique Device Identification System

One of the main problems with the control and safety of medical and in vitro diagnostic devices within the IMDD, MDD and IVD[8,9,10] was the lack of vigilance and post market surveillance that related to problems with devices and reports made regarding devices from their production to the end user[135,144)]. This lack of vigilance and surveillance made it difficult to analyse device faults and ensure that all the devices, experiencing a fault or a problem were identified, and other devices, affected with similar problems or faults, were located to enable them to be rectified or removed from use. The public did not have full access to the data relating to device problems or faults, as it was either not available or incomplete. A full analysis of device problems or faults could not be undertaken for a number of reasons: the data was incomplete, not recorded in a standard format or only accessible with the permission of the manufacturer, agent or competent authority of a given county[105,106].

The new device legislation and requirements introduced a system to identify, individually, a medical or in vitro diagnostic device. This system is known as the Unique Device Identification (UDI), system. This UDI system, once fully implanted, will help in the traceability of devices, enable simpler and more effective incident reporting, improve anti-counterfeiting of devices and ensure that device warning notices are given to the correct end users[134,137,144].

The databases containing the information relating to these devices, their problems and faults will be available for review by relevant authorities and some of the data will be made available to the public[138]. This public data will be maintained and issued via the European Databank on Medical Devices, EUDAMED[193].

By introducing the UDI system in respect of medical devices and in vitro diagnostic devices, the EU regulations and UK legislation were brought up to date, and in line,

with similar regulations throughout the world. [134,139,149)]. The requirements for a UDI number on a medical or in vitro diagnostic device is to be phased in over a number of years[(141,142)] as shown in figure 4.3 and figure 4.4 respectively[(143)].

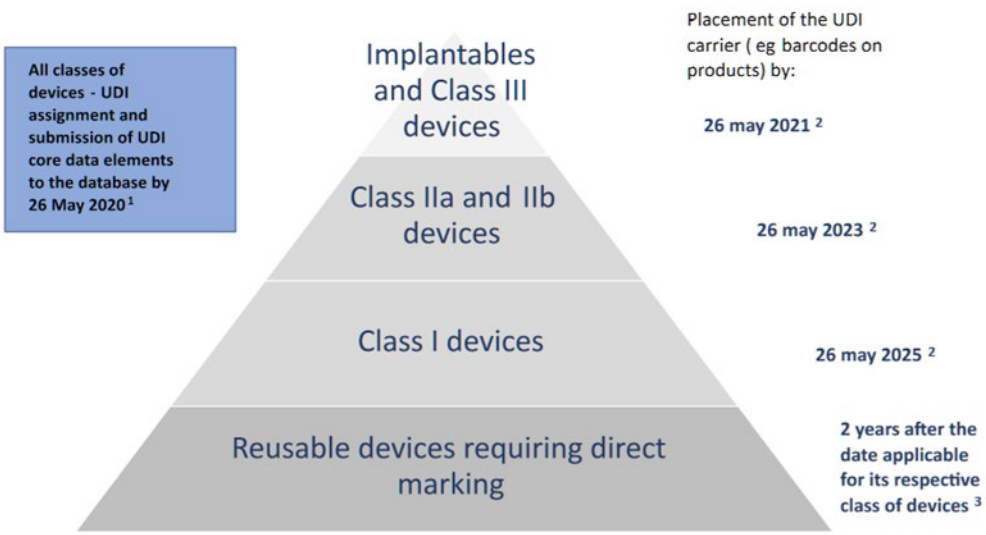


Figure 4.3 Time line for UDI implementation for Medical Devices.

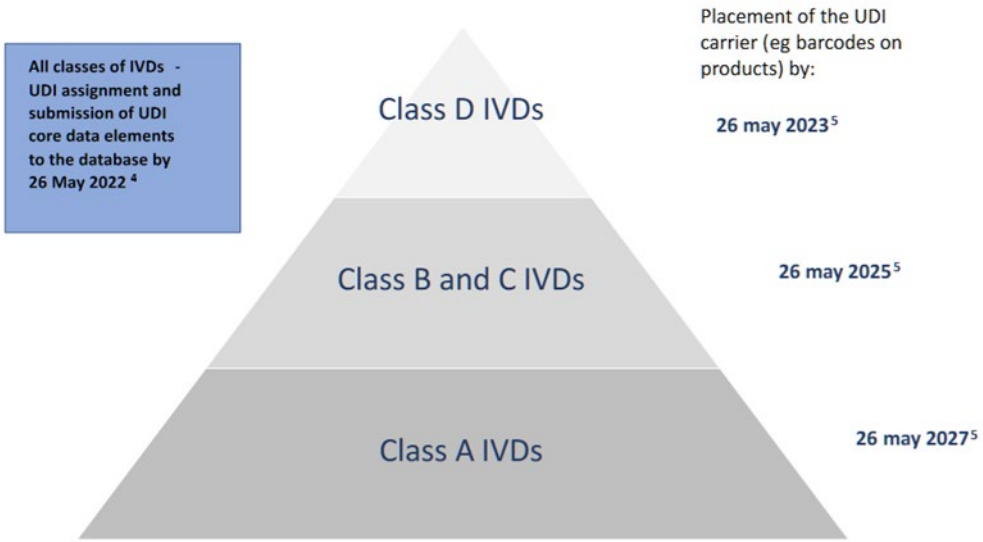


Figure 4.4 Time line for UDI implementation for In Vitro Diagnostic Devices.

4.10.2 What is the Unique Device Identifier?

The UDI is not another serial number, but comprises of three identifiers, all linked to each other to enable the device to be uniquely identified: the manufacturer, the make and model number and the production identification of the device.

These three parts of the UDI are the Basic UDI, the Universal Device Identification – Device Identifier (UDI-DI), and the Universal Device Identification – Production Identifier (UDI – PI) [145,147,148,149,151]. The Basic UDI does not go on the device or product. The combined UDI-DI and UDI-PI will appear on the packaging and will give full information relating to the device, manufacturing site and if required the manufacturing date. (Please note that more information on the EU implementation of UDI can be found in the links given in ref 150.)

4.10.2.1 The Basic UDI-DI

This is the link between all devices of the same type, root design or base chemistry, risk class and manufacturing. Hence, all implantable defibrillators, using lithium batteries, could be assigned the same Basic UDI-DI. Similarly, pregnancy test kits, using the same chemistry and manufacturing processes, could be assigned the same Basic UDI. If a device has two functions, it will have a unique Basic UDI which incorporates those two functions, and not two Basic UDI's for each function. As such, the Basic UDI will link all devices having the same functions and characteristics. By linking devices in this manner, an analysis of device faults and problems will be permitted, areas where a manufacturer, or third party supplier of devices is failing to meet the required performance levels will be highlighted and the public will be able to review device information prior to purchase. The certificate of conformity for a device will state the Basic UDI-DI for the device.

4.10.2.2 The UDI-DI

The UDI-DI contains sufficient details to enable the device to be traced back to the manufacturer of the device and the device type, model or code identifier.

4.10.2.3 The UDI PI

The UDI-PI contains the details of the actual device production - lot and/or serial number, manufacturing date, use by date and software identifier.

4.10.3 UDI Structure and use

The structure of the system is, in some ways simple, and in other ways confusing.

For devices of one type, you have a single Basic UDI Identifier.

Under this Basic UDI identifier, you can have a number of Device Identifiers, different manufacturers, units of different colours, etc.

Under the Device Identifier, you will have one or more Production Identifiers – one for each batch, lot or serial number.

So, a pyramid of numbers is produced, which allows each device that has been manufactured to be identified back to its manufacturer and the date of being manufactured. The pyramid also allows data, for all similar devices, to be collected in a central database, by virtue of the Basic UDI identifier.

This central database for EU and UK devices is known as the European Databank for Medical Devices (EUDAMED). This database was supposed to be functional in 2020 but has now been delayed to 2022. Until then, and at the time of writing this thesis, those individuals or bodies placing devices on the market must apply to the 'local' competent authority for a Single Registration Number.

There are four bodies currently authorised to issue and control the use of UDI numbers these are[(152)]:

1. GS1 (Global Standard One),
2. HIBCC (Health Industry Business Communications Council),
3. ICCBBA (International Council for Commonality in Blood Banking Automation),
4. IFA GmbH (Informationsstelle für Arzneispezialitäten).

These four bodies will supply information to the EU central database.

4.10.4 Identification for 'in-house' designed and manufactured devices.

The above requirements for labelling are in some ways rather complex and involved but necessary to meet the regulatory requirements. They are also rather expensive for one off or low number manufacturing such as undertaken within a health care institution.

The rules detailing the identification of devices manufactured 'in-house' and for 'in-house' use only are rather vague. The exemptions given in both EU and UK legislation detail that devices manufactured for 'in-house' use by a health care institution should provide 'the details necessary to identify the devices'. So, the full UDI identification system does not require to be used provided the devices are uniquely identified.

4.10.4.1 Identification of 'In-House' Medical Devices

Devices designed and manufactured within a health care institution are normally manufactured for a specific need or application. These devices are usually a 'one off 'or produced in very low numbers. It will be remembered that , the exemptions state that 'in-house' manufacture shall not be 'on an industrial scale'. Medical devices which are manufactured for 'in-house' use, within NHS Tayside, are either manufactured within the Department of Medical Physics or in conjunction with this department. Each device that is manufactured prior to being issued to the user is given a Medical Physics asset identifier. This identifier is logged into the NHS Tayside Asset Management register. The register includes such details as the device user and user location, location of design documentation (including the technical files), and, if required, service and maintenance schedules. Each device is given a unique asset identifier, even if more than one of the specified device is manufactured. Other identification details of the device may also be kept on file e.g. software version, photograph and model number.

4.10.4.2 Identification of 'In-House' In Vitro Diagnostic Devices.

These are developed by the HMFUS department. Any IVDD developed is identified by its batch manufacture reference. The batch manufacture documentation also details the user and user location. The batch manufacture documentation contains

all the details necessary to manufacture the IVDD, including manufacture process, material lot and identifier information and the final test results.

4.11 Responsible Person or Persons

The EU legislation[2,3], at Article 15, and the UK legislation[4], at paragraphs 80 and 149, introduce a new requirement for manufacturers, distributors and those individuals or bodies acting as agents, to have a '*Person responsible for regulatory compliance*', a PPRC. This person or persons must be appropriately qualified and experienced in regulatory matters, and have the authority and responsibility to influence and control, the organisation's regulatory compliance to relevant legislation[153].

The persons responsible for regulatory compliance (PRRC) cannot act for both the manufacturer and distributors or agents; they must be separate individuals. For small or micro businesses[154], the role of the PRRC can be outsourced or shared between a numbers of such businesses, as long as there are no conflicts of interests between the work undertaken by these businesses.

4.11.1 Required Qualifications and Experience

The qualifications required for the role of responsible person or persons are a university degree or equivalent course of study in law, medicine, pharmacy, engineering or another appropriate scientific discipline, and at least one year of professional experience in quality or regulatory work for medical devices, or, four years professional experience in quality or regulatory work for medical devices[153,155].

4.11.2 Person Responsible for Regulatory Compliance within Health Care Institutions.

There appears to be no legal basis for a PRRC within Health Care Institutions, under the exemptions for health care institutions. This does not mean that such a person or persons is/are not required. A PRRC or several PRRCs should be nominated as the exemptions require the health care institution to produce documentation to satisfy the exemption requirements, maintain and update data that can be viewed by the public and ensure that 'post market surveillance', as detailed in the legislation, is undertaken and can be a point of reference for the relevant authority and members of the public. The PRRC must also maintain an oversight of the regulatory requirements, and review the quality systems, applicable within the

health care institution, and used in the design, development and manufacture of devices, to ensure that they continue to meet the changes in the regulatory or associated standards.

Within a health care institution, it may be necessary to have a small group of PRRCs as a health care institution may design and manufacture various types of both medical and in vitro diagnostic devices. These devices may not all use the same science, technology or chemistry and some may, in fact, be software devices. Accordingly, a number of individuals, with different knowledge and experience, will be required to ensure these various devices meet regulatory requirements.

4.12 Software used as a medical device or in vitro diagnostic device

The previous legislation covering in vitro devices mentioned software four times, but did not specify control or risk factors for the software. The legislation in the old medical device directive referred to software twice and stated that it was to be classified as being in the same risk class as the device it was to be used in or with. By contrast, the new UK legislation mentions software 88 times, the IVDR 44 times and the MDR 48 times.

Schedules 3 and 17 of the UK requirements, (which are the same as the EU MDR and IVDR requirements) refer to ‘Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves’. Software could range from being a simple spread sheet, which is used to calculate drug dose from a person’s mass, height, age, etc to a full radiotherapy beam planning system.

The risk classification of such software will either be the same as the device it is associated with or, if independent software, be classified as a standalone device and the derived risk classification will be the highest risk class associated with the use of the software. Risk Classification Rule 11 for medical device risk classification in both UK and EU medical device legislation, details the risk levels for software. The implementation rules for in vitro diagnostic devices informs that independent software is classified in its own right.

The risk classification is dependent on the device type is it an medical device or is it an in vitro diagnostic device[(158)].

The standard BS EN 62304:2006+A1: *Medical device software. Software life-cycle processes*[156], details the procedure for medical device software development and maintenance. This standard defines three software safety classes:

'Class A: the software cannot cause any harm
Class B: the software can cause minor harm such as injuries
Class C: the software can cause major harm such as severe injuries or even death'

These definition of safety classes may assist in the risk classification of the software[157]

The risk classification will influence how the software is implemented and tested.

The level of detail concerning the software contained in the technical file and the user information will, also, be dependent on the risk classification of the device.

Software will require a UDI if it is classed in its own right as a device[160].

The documentation issued to users of software must contain details of the minimum requirements of both operating hardware and associated software, that is – operating system, processor and memory requirements, display and input device, etc.

Any software developed as an 'in-house' device or for use within an 'in-house' device must follow industry standards for its design and development. Software should undergo the same rigorous design, development and testing processes as the other parts of the device being developed. Standalone software must be treated as if it were a device – and so technical documentation must be produced, testing must be carried out and external assessment as per the risk classification of the software must be undertaken.

These new requirements will have an impact on the development of software applications as they will have to meet the full requirements of the relevant device legislation. For example, simple spreadsheets have now been classified as medical devices or in vitro diagnostic devices. A simple programme which takes some basic patient parameters, for example, height, weight and sex then uses this information to calculate a drug dose, could be classified as a medical device, and depending on the drug being dispensed, will influence the final risk classification of the software.

Chapter 5 CASE STUDY

Academics at Dundee University have been working on a prototype OCE system since 2012[160,161,162]. This prototype system has been developed to determine if the combined use of optical coherence tomography and elastography could be used to the review prostrate samples for possible signs of cancerous nodules in real time.

As previously described, one of the aims of this thesis was to review the OCE system to determine if it was fit and safe for clinical use within NHS Tayside . This review determined that guidelines were needed to ensure medical and in vitro diagnostic devices, resulting from academic research and development, would meet the requirements of UK legislation. These guidelines would specifically relate only to devices manufactured for 'in-house' use within NHS Tayside.

5.1 Background to the OCE project.

The initial trial of the OCE system[170], was carried out by analysing prostrate biopsy samples prior to clinical review and reporting by a pathologist. The samples were transported from the urology theatre to a university laboratory within Ninewells hospital. Once the samples had been scanned, they were returned to the theatre, and finally sent to pathology for analysis and reporting of results. This multi-step process was required as the OCE system was classified as a research device, and had not been fully tested, or checked, for use within clinical areas.

Analysis of the data collected showed that there was a good correlation between the results from the OCE system and the pathology results [79,170]. Although this first study only comprised of 10 subjects, the promising results shown, were sufficient to justify a follow-up study. This study would involve a larger cohort of patients, and the findings from this research, would, hopefully, validate the previous results.

It was noted that to enable larger number of samples to be evaluated, it was important that the OCE system was located within the areas adjacent to the urology operating theatre.

5.2 Initial review of OCE system

5.2.1 OCE Review Process

A risk assessment of the OCE system was needed, prior to it being located within the urology theatre area. This assessment was carried out by staff of the Medical Physics Department (MPD) of NHS Tayside, to ensure it was safe, and fit for use within a clinical area.

The review looked at the documentation relating to the OCE system and, in particular, the user information, the information relating to the system calibration, repair and maintenance. An additional review would also be needed, to assess the possible risk due to the construction of the system, or emissions being produced by the system, for example optical, acoustic or radiation emissions. Prior to the system being used within a clinical area, it would also need to be assessed by the infection control department of NHS Tayside. This assessment would ensure that the device would be cleaned, using appropriate methods, and that the use of the device would not pose any infection control hazards.

The results of this review should indicate any modifications required and the documentation to be produced, to enable the OCE system, to be signed off as fit for use within NHS Tayside.

5.2.2 Review findings

The OCE system consisted of a control computer, (including keyboard, mouse and display monitor), an anti-vibration table supporting the optical coherence system and required laser source. The Elastography sample vibration system was mounted on a three axis movement, which was also located on the anti-vibration table. The sample vibration system was driven by an external signal source and coupled to an external power amplifier.

5.2.2.1 Electrical and electronic construction and safety.

A review of the electronics identified the following concerns regarding the safety of the OCE system:

- The electrical connections within the OCE system were haphazard, unsecured, and not terminated correctly.

- The electronic layout needed to be rationalised, in particular the location of the PC, keyboard and monitor.
- The power amplifier and signal generator used to power the sample vibration system was not secured.
- The laser, associated with the device, was not secured, and no local rules or risk assessment was available
- The power adaptors used, had not been secured and the complete system had never been electrically safety tested.

The staff, responsible for electronics at the Medical Physic department and who had been assigned to oversee this project, rewired: the control system, the driver for the sample vibration system and the PC control interface. The mains power distribution was reconfigured and the superfluous/unnecessary mains extensions, were removed.

Further work, which was undertaken included, adjusting the wiring from the control PC so that it was simplified, rerouted, shortened and correctly terminated. Trunking was used, where possible, for external cabling and wiring. It was also noted, that the power amplifier, driving the sample vibration system, was overrated for its application.

On completion of this corrective work, the system was safety tested to ensure it met the requirements of 'BS EN 61010-2-101:2002 Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment'[(163)].

5.2.2.2 Mechanical construction and device stability.

A review of the systems mechanics would ensure that the manufacture and construction of the device was safe, i.e. that there were no exposed live electrical parts, no exposed sharp edges and no hazardous detachable components. The review would also identify any risk to the operator due to the size and weight of the system.

The OCE system's stability was not of concern as the OCE system's weight distribution brought its centre of gravity closer to the ground. However, the table,

supporting the amplifier and signal generator was tall, with a small footprint, which would cause stability concerns. The wheels on this table were small in diameter, making the table difficult to steer and hard to get over expansion joints and manoeuvre into lifts. To overcome this, a lower and larger table was found and modified to hold the amplifier and frequency generator. This table had larger diameter wheels fitted to ensure ease of movement.

It was noted that a number of the enclosure covers were missing. These were remade and fitted to the system protect the OCE assembly and components from being tampered with, to reduce the ingress of dirt and to improve the ease of cleaning the system. Additional support brackets were produced to ensure the sample vibration system, and the laser light source, were securely attached to the optical platform. Finally, the computer display and keyboard were replaced with medical grade touch screen monitor.

5.2.2.3 Optical and acoustic radiation/emission and safety.

During the review of the OCE system, it was noted, that when in use, the sample vibration system produced significant levels of acoustic noise. Acoustic absorbing material was fitted to the inside of the enclosure, to reduce these noise emissions.

An initial risk assessment of the laser source was based on information obtained from the manufacturer. This information stated the source was ‘eye safe’, and, therefore no additional safety precautions (for example remote interlock or laser warning labels) were required. However, a risk assessment of the laser was undertaken by NHS Tayside’s non-ionising radiation protection officer, who found that there was a requirement for both the use of an interlock, as well as displaying appropriate hazard warning labels.

5.2.2.4 Infection Control requirements.

The infection control department of NHS Tayside carried out a review of the OCE system after the above remedial work was completed. This report stated, that the improvements made by upgrading the monitor and trunking, would allow the system to be easily cleaned and, therefore, comply with infection control requirements.

However, it was noted that cleaning and decontamination instructions would need to be produced, and if possible, to manufacture covers for the partially open base of the unit. In addition, a review of the area containing the actual sample and sample vibration system was carried out to prevent possible contamination from the biopsy sample or preserving fluids. Clear instructions on how to protect the biopsy sample during the scanning process would also need to be given in the user instructions.

5.2.2.5 OCE System Documentation

This was an area of concern for those reviewing the OCE system, as there was little, or no information, relating to the actual system. The documentation reviewed included numerous academic papers about the system but, vital documentation including the user guide, calibration status, hazard identification and construction guide, had not be written. As there was no ethically approved protocol for the proposed follow up clinical trial, any work involving patient samples, should not be undertaken until this had been completed and the required ethical approval, given.

5.3 Rational for a Case Study

This lack of documentation would prevent the system from being risk assessed, and, therefore, it could not be used within clinical areas. As detailed in the aims of this thesis, the OCE system would be reviewed as a case study, to determine what documentation would be necessary to ensure that the OCE system would meet the requirements of the exemptions, detailed in the UK legislation[(4)] for any 'in-house' manufactured device.

Following this review, guidelines would be produced for use by M&H or when working in collaboration with academics or third parties, during the design and manufacture of medical or in vitro diagnostic devices for 'in-house' use, so as to ensure that they are correctly controlled and documented. Further, by following these guidelines, the exemption requirements, detailed in UK law, for 'in-house' manufactured device, would be met. Any devices meeting these exemptions requirements would also meet the requirements of NHS Tayside.

5.3.1 Case study outline

The outcome of this case study would be the drawing up of guidelines for those individuals, working on academic projects, to ensure they are correctly controlled and documented. These guidelines, if followed, would result in medical or in vitro diagnostic devices meeting the requirements of the exemptions detailed in the UK legislation[4] paragraphs 71 and 140 for 'in-house' manufactured devices. The guidelines would also ensure, that the documentation required to demonstrate that the exemption requirements have been met, is produced. To simplify matters, a device, by meeting these exemption requirements, should also meet the requirements of NHS Tayside.

5.3.2 Case Study Plan

To achieve the primary aim of this thesis the following actions were to be undertaken.

- To review the exemptions contained in the UK legislation[4] relating to the 'in-house' manufacture of medical and in vitro diagnostic devices, in order to determine what documentation needed to be produced and which actions were required, to meet these exemption requirements.
- To produce the documentation required to show that the OCE system met the legislative exemptions.
- To draw up guidelines, for use by the University of Dundee Engineering School, to ensure that these documents were produced in future academic projects related to medical and in vitro diagnostic devices.
- To have the documentation and design files of the OCE system reviewed by M&H QA auditors and, if possible, by external auditors.

5.4 UK Exemption for 'In-House' Manufacture

The exemption requirements for the 'in-house' manufacture of medical and in vitro diagnostic are detailed at paragraph 71 and 140 of the UK legislation(4). The following is a synopsis of these exemptions.

These exemptions relate to devices, manufactured, or modified, within a health care institution for 'in-house' use only. These devices must not be transferred to another body outside the manufacturing health care institution.

Under these exemptions, the GSPRs apply to devices manufactured or modified for 'in-house' use.

The exemptions also require that:

a. A justified reason be given for the need and manufacture or modification of such devices;
b. Proof that these devices are designed and manufactured under a suitable quality system;
c. A declaration, detailing that the device meets the requirements of the exemptions, must be drawn up, and confirms that device is manufactured in accordance to the manufacturing documentation detailed in point d below. The declaration must also detail how to identify the device and give the contact details of the manufacturing health institution.
d. The documented details of the device, should state: the intended purpose and performance of the device, how it works or is to be used, how it is manufactured and maintained so as to be fit for use, and details given as to how it meets the relevant general safety and performance requirements.
e. The details of how experience gained in clinical use will be gathered, evaluated and acted upon.

Again, it must be noted, that these exemptions are not to be used to manufacture devices on an industrial scale. The term 'industrial scale' will be assessed on the basis of the number of 'in-house' devices produced in relation to the number of equivalent commercial devices which are produced.

5.4.1 Exemption Documentation.

5.4.1.1 Justification

The justification for the manufacture or modification of the device must detail why no other device, currently available for purchase, will provide the functionality or test required. The justification must inform as to the desired outcome of the device or device modification and why there is an important but significant unmet clinical or medical need.

5.4.1.2 Proof of Quality System Used

The evidence that the device has been manufactured under an appropriate quality system must be provided. This could be evidence of accreditation to an appropriate quality standard or a full description of the quality system used.

5.4.1.3 Device details

In the description of the device, the details should include, the purpose of the device, the intended users and patient group, how it functions and the performance criteria of the device. User instructions must be included and outline the maintenance of the device, appropriate cleaning instructions (including sterilisation instructions if applicable), calibration or quality checks required, troubleshooting advice and, in the event of a device failure, who to contact.

Many of these details will/should be obtained from the evidence generated when addressing the General Safety and Performance Requirements (GSPR).

5.4.1.4 General Safety and Performance Requirements

Prior to addressing the GSPRs, the device type/class must be determined to ensure that the correct device risk classification is ascertained. Once the device type and its' risk classification are known, then the GSPRs can be addressed.

The risk classification rules which need to be followed will be dependent on whether the device is a medical device or an in vitro diagnostic device. The definitions given in the UK legislation[4] and the EU Regulations[2,3] can be used to determine if the device is a medical device or an in vitro diagnostic device.

As stated, once the device type is known then the risk classification of the device can be determined. This can be accomplished by following the appropriate classification rules. The rational for the final device classification must be documented.

Evidence of how each GSPR, has been or will be met, must be documented The document must detail whether the requirement is applicable, details of how the requirement is to be fulfilled, or why it is not applicable, and the storage location of the evidence detailing how the requirement has been met. Table 5.1 is an extract of the draft GSPR document produced for the OCE system. The information contained in the documents produced to address the GSPRs will be used to address the exemption requirements.

The draft GSPR matrix for the OCE system is given in Appendix 5.01 '*OCE General Safety and Performance Requirements Matrix*'.

5.4.1.5 A manufacturing file

Written instruction must be provided detailing how the device was manufactured, all acceptance testing undertaken, required labels and suitable packaging required to preserve the integrity of the device. This document should be detailed enough to allow future devices to be produced.

5.4.1.6 Post manufacture and in use feedback

These are the details of how the clinical and user experience will be gathered, evaluated and acted upon. This evidence is not only from the device user feedback, but from, for example, repair and service information, discussion with users and even continuing research in the field of the device leading to device improvements. This documentation must detail when to contact the relevant authorities, when to produce any required feedback reports and what actions are to be taken, if the device is involved in a serious incident.

5.4.1.7 Declaration

This is a declaration that the device meets the requirements of the exemptions. The declaration will contain a brief explanation of why the device or modification is required, how the device can be identified, and the details of the quality system used

to control the manufacture of the device. The declaration will state the location of the documentation to support this claim. The declaration will be signed by a responsible manager of the relevant health care institution, who will give their contact details and also the details of who should be contacted for further information or assistance, relating to the device, if required. Note that a responsible manager will need to be somebody with the legal authority to sign on behalf of the health care institution, the collaborating university or third party.

Table 5.1 Extract of the Draft General Safety and Performance Matrix for the OCE system.

Essential Requirement	A NA	Standard	Supporting Documentation	Location of supporting documentation
6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.	A	EN ISO 14971:2012/2019 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	WIRD05 Risk Analysis Correct use details found in the user manual.	OCE user manual held in Q-Pulse . As this is a prototype device and under development this area needs to be reviewed after each modification or change both hardware and software.
7. Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.	A	IVDR BS EN 60601-1 and BS EN 61010 – and associated standards	OCE Technical File	OCE technical file retained in – Q-Pulse.
8. All known and foreseeable risks, and any undesirable effects shall be minimised and be acceptable when weighed against the evaluated potential benefits to the patients and/or the user arising from the intended performance of the device during normal conditions of use.		EN ISO 14971:2012/2019 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	WIRD05 Risk Analysis. Residual risks detailed in the user manual.	OCE user manual held in Q-Pulse .

5.4.2 Publicly available information

The exemption requirements detail the information which needs to be made available to the public. This information will include contact details of the institution, (and the relevant contact details of the department responsible for the device), details that are necessary to identify the device, a declaration that the device meets the GSPR and the rational for any of the requirements deemed not to be applicable. All of this information can be gleaned from the documentation referred to in section 5.4.1 '*Exemption Documentation*'.

5.4.3 The OCE documentation Review and the Documentation Required.

This review was undertaken to determine if any of the available OCE system documentation could be used to meet the exemption requirements of the UK law.

5.4.3.1 Documentation review outcome

The review determined that only academic papers had been produced for the OCE system. Some of these papers did have technical and user information relating to the device, but this information was not sufficient for the purposes of the exemption requirements.

The classification of the OCE system was not stated in any of the academic papers – in short, was it a medical device or was it an in vitro diagnostic device? As previously stated, this basic, but important information determines which set of risk classification rules are to be followed and which of the GSPRs are to be reviewed and met.

Further there was no documentation detailing how the OCE system was assembled or the parts used in its manufacture, nor were there any details of how to set up or calibrate the system. Also omitted, were the details of the maximum or minimum size or physical volume of the samples to be scanned, the resolution of the scanned image was not stated, no validation of the elastography results had been undertaken nor an understanding of the ability of the system to differentiate between the areas of different stiffness within the samples. If the device failed the published thesis, and supporting papers, did not contain enough detailed information to enable the device to be repaired.

In addition, there was no information as to how to use the device, how the data obtained from the analysis would be stored within the patient‘s medical file, nor how the analysis of the scanned images was undertaken. The only people with sufficient knowledge as to how to operate the OCE system, were the academic staff who had carried out the work on the system and those individuals supervising this work. If any other person was required to operate the OCE system then, in order to do so, they would have had to seek assistance from these members of staff. Without their assistance/input, the OCE system could not be operated by anyone else.

It was also noted that no risk assessment nor hazard reduction analysis nor review had been undertaken to determine the safety of the OCE system. This meant that essential data/information was unavailable, for example there was no indication of possible contra-indications to the use of the system, the hazards arising during the use of the system were unknown, the optical hazard from the laser used in the OCE system, had not been checked and the risk, associated with the contamination of the sample placement area, was also unknown.

Lastly, there was no documentation detailing how the OCE system met the Essential Requirements of the old regulations.

5.5 OCE system - Exemption Requirements Documentation to be produced

The following is the list of documents to be drawn up to directly address the exemption requirements or to enable these requirements to be met in respect of the OCE system.

1. Justification that the OCE system provides a function not yet met by another device available on the market.
2. Evidence of an appropriate quality system.
3. Classification of the OCE system.
4. Completed GSPR Matrix for the OCE system and documentation to support how the relevant requirements have been or will be fulfilled.
5. A risk and hazard analysis which must detail any residual risks and contraindications to the use of the OCE system. This analysis must also have a formal statement confirming that the device is safe to use.
6. The documentation must detail how the feedback, relating to the OCE system, is gathered, and how this feedback is analysed and reported.
7. How the device is identified, its location tracked while in use and the actions to be taken if the device goes missing.
8. Reports on the clinical and system tests to determine the operation limits of the OCE system e.g. scan resolution, elastography resolution (the ability of the system to differentiate between areas of different stiffness) and the results of clinical trials.
9. Calibration instructions
10. User and cleaning instructions
11. The technical and manufacturing data required to meet the exemption requirements.
12. A declaration that the device meets the UK exemptions.

5.5.1 OCE System Device Type and Risk Classification

5.5.1.1 Device type

During the review of the existing documentation relating to the OCE system, it was found that the device type of the OCE system had not been determined, in other words - was the OCE system a medical device or was it an in vitro diagnostic device? By answering this question, the area of the UK legislation required to be followed, would be determined.

The definition of a medical or an in vitro diagnostic device used is that given by the Global Harmonisation Task Force (GHTF), (evolved into the International Medical Device Regulators Forum (IMDRF))[165] and echoed by the Food and Drug Administration (FDA)[166,167], the EU Regulations[2,3] (Article 2 Definitions Sections) and the UK legislation[4] (Scope and Definitions Sections New Part VIII and New Part IX).

The OCE system requires that a biopsy sample is taken and then scanned to determine the pathology of this sample. This aligns with the definitions of an in vitro medical device. Hence, the risk classification of the device will be based on Schedule 23 Regulation 1A 'Classification Rules for in vitro diagnostic medical devices' of the UK legislation[4].

5.5.1.2 OCE risk classification

The risk classification is required to ensure that the device is designed and manufactured to meet the risk posed by the device during its intended use. The risk classification is also required when determining which of the GSPRs are applicable to the device. The type and level of control, and the reporting of post market feedback, is also dependent on the risk classification of the device. The risk classification for the OCE system can be determined by following WI-RD.07 'WIRD07 Classification Rules IVDR'[102]. By using this work instruction, the OCE system risk classification is found to be **Class C**. This classification is derived as follows:

1. Does not apply as the device is not used for the purposes of determining infection load or infection transmissibility.
2. The devices is not used for compatibility checking.

3. The device is used for screening and in the diagnosis of cancer.
   Applicable – **Class C**
4. Device is not intended for self-testing but near patient testing as per Rule 4 point (5): **Rule 3 still applies**.
5. Not one of these devices.
6. Device is cover by **Rule 3.**
7. Device is cover by **Rule 3**.

See Appendix 5.02 Risk Classification For the OCE System.

5.5.2 General Safety and Performance Requirements Review.

As the OCE is a Class C in vitro diagnostic device, the General Safety and Performance Requirements detailed in SCHEDULE 17 Regulation 1A are to be reviewed, and the documentation produced, to detail how the applicable requirements are met. An explanation of any requirements which are not applicable, must also be provided.

To facilitate this review the matrix, detailed in WI-RD.10 'IVDR General Safety and Performance Requirements Matrix'[(102)], was used. The completed matrix is given in Appendix 5.02. As this device is a prototype, all the documentation referenced in the GSPR matrix and GSPR matrix itself will need to be updated on a regular basis as the OCE system undergoes modifications and improvements.

Points to note from the GSPR review given in Appendix 5.01

Some of the GSPRs have been deemed not applicable. For example the OCE system is not for self-testing, the OCE system does not require packaging nor does it use any reagents to produce a test result.

Due to the OCE system not being a traditional in vitro diagnostic device, the harmonised standards given for in vitro diagnostic devices were supplemented with more applicable standards. For example, the BS EN IEC 60601 family of standard for medical devices was deemed the best fit for the OCE system design and construction. The BS EN IEC 61010 family of standards for laboratory equipment was deemed appropriate to ensure the electrical and mechanical safety of the OCE system.

5.5.3 Risk / Hazard Management and Analysis

The GSPRs for in vitro diagnostic devices are given in UK legislation[4]. In particular, paragraph 3 of Part 1 of Schedule 17 Regulation 1A requires that a risk management system is to be in operation to ensure that risks and hazards are analysed and reduced to an acceptable level prior to putting an in vitro diagnostic device into use. It was noted that no risk / hazard analysis had been carried out on the OCE system.

The risk analysis for any medical or in vitro diagnostic device should start as soon as the device specification is known and agreed. This is to ensure that any risks noted, are taken into account at the start of the design and development phase, rather than trying to include changes, due to risk or hazards, at the end of this phase. Risk analysis reviews should be undertaken throughout the lifetime of a device from the concept phase through to the scrappage of the device. This will ensure that any hazards and /or risks found, no matter at what stage of the life of the device, are reviewed, analysed and reduced to an acceptable level.

BS EN ISO 14971:2019[169] is the harmonised standard for risk in both medical and in vitro diagnostic devices. To enable the risk analysis to be undertaken and documented, M&H work instruction WIRD05 Risk Analysis[102] was followed.

The initial risk analysis for the OCE system is given in Appendix 5.05. The final risk analysis of the system must contain a statement confirming that the use of the OCE system outweighs any residual risks or hazards associated with the OCE system when operated as intended.

All changes to the OCE system must be reviewed to ensure that they do not introduce any new risk or hazard or exacerbate any existing risk or hazard. Similarly, the risk management system must, with respect to risks and hazards, review any feedback from users, patients or others obtained from the post-production and in use phase of the OCE system. The result of all risk and hazard reviews are to be documented and any recommendations acted upon. If the recommendation is that ‘no action’ is required, then this too, must be documented.

5.5.4 Device Feedback and notification control

Another requirement of the legislation to be taken into consideration is the Post Market Performance Follow-up, 'PMPF'. This 'follow-up' requires that the performance of the OCE system is reviewed to ensure that it is functioning correctly, and that the results produced, are clinically correct and as expected. Post market surveillance will be controlled by four new M&H Work Instructions to be produced as a result of the work of this thesis. The work instructions will be:

1. Post Market Surveillance;
2. IVDD Post Market Performance Follow-up;
3. MD Post Market Clinical Follow-up; and
4. Generation of Periodic Safety Update Reports.

5.5.5 Technical, Manufacturing and User Information

The requirements for the technical file, for a fully compliant CE marked device, are detailed in WI-RD-01 'WIRD01 regulatory legislative technical file contents' [(102)]. Section 2 of this WI outlines the technical file contents for an IVDD. This work instruction is derived from Schedule 18 of the UK legislation[(4)] and Annex II of EU IVDR regulation[(3)]. As this is a prototype 'in-house' device, some of the requirements have been deemed not applicable, or the requirement is amended, to meet the requirements of the exemption. Table 5.2 is a list the documentation required by the exemptions to be produced for the OCE system. Once completed, this documentation will be held, either in the OCE system technical file retained in Q-Pulse, or its location will be given in this technical file. (Note Q-Pulse is a commercial application used within Medical Physics to control and manage documentation and activities associated with the M&H quality system.)

As the OCE system is a device for 'in-house' use only, the certificate of conformity is not required, but a declaration, that the device meets the requirements of the exemptions, is required.

Table 5.2 Documentation required as proof the OCE system meets exemption requirements

Requirement	Applicable YES/NO	Reason for non-applicability or description of
Title, Index and Certificate of Conformity.	Yes	Need a certificate to inform that the device meets the requirements of the exemptions.
Device Description, Variants, Accessories and Specification	Yes	Outline of the function of the OCE and a device specification is required.
Information supplied by the Manufacturer	Yes	Full user instructions including labelling description, cleaning instructions, calibration details, residual risks/hazards related to OCE system use and safety information.
Design and Manufacturing Information	Yes	A general description of the steps taken to design and develop the device. More detailed information on how the OCE system work. Full details of how to manufacture the OCE – parts lists, wiring diagrams, mechanical drawings, tests to be carried out, all software to be loaded and how tested, final test and calibration checks.
General Safety and Performance Requirements	Yes	The General Safety and Performance Requirements Matrix
Risk/Benefit Analysis and Risk Management	Yes	Output from WIRD.05 risk and hazard assessment
Product Verification and Validation	Yes	This information contained in the design and manufacturing documentation. Also this information

		not as extensive as this is still a prototype device and not all testing on the performance of the device is completed.
Device Performance	Yes	The evolution of the device performance is still ongoing and hence this section can only detail the various comparisons carried out so far between biopsies scanned on the OCE and then sent to pathology for review. Work still to be carried out is to determine is the minimum dimension/volume of sample to be scanned and if the method used to obtain the sample affects the scanning result.
Device Accuracy	Yes	Determination of device accuracy still ongoing. So can only detail the testing being carried out and the optical calibration using the calibrated test plate.
Clinical Performance and Clinical Evidence	Yes	Details of testing methods and result evaluations of all tests carried out to determine the performance and efficacy of the OCE system. How these are reviewed and reported.
Stability	Yes	How was the OCE working life time determined and verified? Note For a chemical/biological based IVDD this will be the stability of the actual chemical/biological mix both in use and pre-use – storage, shipping and shelf life.

Software Validation and Verification	Yes	The information relating to the bespoke software and algorithms written to enable the OCE to operate and produce scan data. How this was tested and results verified.
Additional Information	No	
Quality System	Yes	A note in the certification to state the OCE system was designed and manufactured under a system complainant to 13485:2016 and aspects of the work, as defined, are as required by 15189:2012.
Standards	Yes	A list of standards followed to be given on the certification.
Self-testing Devices	No	This is not a self-testing device.
Changes and additions	Yes	All changes and additions are controlled via QP.01 and logged in the Q-Pulse system
Post Market Surveillance Plan	Yes	Reduced post market surveillance plan but it most include details of how all feedback, experienced gained from device use and incidents relating to the OCE system will be gathered and reviewed to determine if they are reportable to external authorities

5.5.6 User and cleaning instructions

Two of the most important documents to be produced are the User Instruction and the Cleaning Instructions.

The remit of those working on academic projects is to produce academic papers. The technical and scientific information contained relating to any device manufactured is often not complete, and the information as to how to use the device is either lacking, or non-existent. If projects developing devices are to be continued, then those working on these projects should pass on technical and scientific information to their successors. They should also instruct their successors on the operation of any devices made and how to interpret the information any such devices produce. In many cases this information is either not passed on, or is lost. Without this basic information the device is no longer usable, and time has to be spent, regaining the knowledge to use the device and interpret any output from the device. The details required to meet the GSPR will also outline details how to use a device, interpret the output from the device as well as, maintain, repair and clean the device.

The draft user instructions, given in appendix 5.06, were drawn up following the requirements detailed in the GSPR relating to the information to be contained in the user instructions.

Cleaning instructions must also be produced in respect to a device. Without these cleaning instructions the OCE system will not pass the inspection carried out by the NHS Tayside infection control team. The team will need to see and review the cleaning instructions to ensure users can clean, or if required, sterilise the devices. The team will determine if these instructions are sufficient. (As an aside, even if the device was only to be used in a laboratory setting, the method of cleaning the device must be validated and documented).

The OCE system may be used to scan biopsy samples. In these cases, the cleaning instructions for the OCE system must include instructions on how to clean the area within the sample scanning area. These instructions are required in case a sample falls, or any sample fluid is spilt in this area. These cleaning instructions should be contained in the user instruction.

5.5.7 Calibration instructions

The exemptions for devices manufactured ‘in-house’ require that these devices are safe and fit for use over the foreseen lifetime of the device. To ensure that the OCE system is fit for use, the output from the scanning system should be periodically checked to ensure that the image produced is correct and that the Elastography system is able to detect the small changes in stiffness required to highlight the difference between normal cell formations, and cancerous cell nodules. While reviewing the OCE system it was found, that there were no instructions for the calibration, or checking, of the device’s scanning function. The only check that could be found, was one relating to the scanning of human hair. This showed that the OCE system could scan very small objects but it did not inform as to the accuracy of the dimensional image produced, nor to the ability of the device to differentiate between differences in elasticity within a scanned sample. These checks of the OCE system are still to be determined and tested.

5.5.8 Declaration that the device meets the UK exemptions.

The information required in this declaration is set out in paragraph 140, of the UK legislation(4), ‘Placing on the market and putting into service’ part (5) subsection (f). The information required is set out in 5.4.2 ‘Publicly available information’

The declaration drawn up for the OCE system is shown in Appendix 5.01. Again it should be noted that this declaration is to be publicly available; possibly via the University of Dundee and / or NHS Tayside public web sites.

5.5.9 Review of ongoing changes to the OCE System

Those individuals working on this project, must ensure that any changes to the OCE system are reflected in the documentation produced, including the manufacturing data for changes to the hardware or software, updates to the risk and hazard review documentation, test reports, changes to device calibration and test methods and the user manual.

5.5.10 Conditions of use.

This is not a requirement of the exemptions. These ‘conditions of use’ are there to inform the device users that the device is not to be transferred, or used outside of NHS Tayside. The conditions of use also detail the cleaning instructions, specifically the details on how to identify the device and as required user instructions. The conditions of use are authorised by the senior Clinical Engineering management, the senior clinical or medical staff responsible for the use of the device and the senior infection control staff.

5.6 Guidelines for academic and third party work

After the work, to ensure that the OCE system met the exemption requirements of the UK legislation, was completed, it was determined that guidelines should be produced to ensure that devices resulting from academic, or other third party work would meet the exemption requirements of the UK legislation. These guidelines needed to be easy to follow, fitted in with the requirements of an academic thesis, resulted in the correct documentation being produced, and ensured that the devices produced, met all the safety and documentation requirements of the legislation.

The usual content of a thesis consists of 4 key elements:

1. an introduction to the work to be carried out,
2. the background, including a literature review, to the science and engineering of the work to be carried out,
3. a section detailing the actual work/research carried out and
4. the final section giving a summary of the results of the project and any recommendations for future work.

The exemptions required by the UK legislation to allow devices to be developed and manufactured, by those working in or for a health care institution, require a number of elements. In summary, the following are required:

1. A full justification of why a device which carries out the function to be developed, cannot be purchased;
2. Full details of how the device functions or operates, the evidence that the General Safety and Performance Requirements, where possible, have been met along with the supporting evidence, the manufacturing and production documentation and details of how the information relating to the device is gathered and analysed and:
3. a declaration that the device meets the exemption requirements.

5.6.1 Outline of the proposed guidelines

The following is an outline of how the three main elements of the exemption requirements are included into the four elements/parts of a thesis and thus form the basis of the academic guidelines.

5.6.2 Thesis Introduction

The introduction will need to be expanded –

- to include a brief overview of the device being researched,
- state whether this device is intended be used 'in house' within NHS Tayside,
- specify the target patient group for the device; and
- clarify whether the device is a medical device or an in vitro diagnostic device.

If the thesis relates to a specific area or function of a device, an outline of how the work of the thesis will be used in the completed device should be given.

5.6.3 Thesis Background/Literature Review

For a thesis relating to a device to be manufactured for use within NHS Tayside this section will need to be expanded to include an analysis of the relevant medical or in vitro diagnostic device market to show that the device being developed meets a need not currently available. In the case of the OCE system, it has been shown that there are no devices on the market providing a similar function as the OCE system: - see section 2.3.6 '*Optical Coherence Elastography commercial devices*'.

5.6.4 Thesis Main Body

The main body of the thesis will need to include details of how each of the exemption requirements, relating to 'in-house' manufacture and use, have been addressed and documented. Any requirements not addressed, will need to be detailed in the conclusion section of the thesis.

5.6.5 Thesis Conclusion

The conclusion will need to indicate which of the exemption requirements been met and what documentation has been produced, to show compliance with these requirements. The conclusion must detail what further work is required to enable a device to meet the exemption requirements in full.

5.6.6 Storage of Documentation

A large amount of documentation is normally produced to cover the exemption requirements of any medical or in vitro diagnostic device.

M&H will need to retain a final copy of any thesis relating to devices manufactured for use within NHS Tayside. A copy of the documentation, referenced in these theses which are related to the exemptions requirements for 'in-house' manufacture, will also need to be retained by M&H within the M&H quality system. By retaining all the documentation relating to such devices, M&H will have the full knowledge of these devices and will, when required, be able to request that that documentation is reviewed and amended. As the documentation will be retained within the M&H quality system the retention period, accuracy, method, backup, and document control, for example, will also be fully controlled.

5.7 Proposed M&H documentation to control collaborative work with academic and third parties on medical and in vitro diagnostic devices

The work of university academics related to the design and manufacture of medical or in vitro diagnostic devices must adhere to appropriate quality standards. The university may wish to implement a quality system. To achieve this requirement, such future projects could be undertaken in collaboration with an organisation which has operates an appropriate quality system. By doing this, the work would then be under the control of an appropriate quality system. The external organisation, in conjunction with the university, would need to draw up, the appropriate documentation to control such work.

The following details the proposed Quality Documentation to be used by M&H to control work in collaboration with university academics and third parties.

5.7.1 Documentation: Goals and Overview

The proposed control documentation is required to ensure that the manufacture of devices, by an academic or third party meets the exemption requirements of the UK legislation related to medical and in vitro diagnostic devices[(4)]. The relevant parts of such work must be undertaken under the auspices of a suitable quality system[(4)].

The control documentation to be simple, effective, and not impair innovation or research. The documentation to be written in plain English – not technical, not 'QA speak'.

This documentation is to control the development of devices for use within NHS Tayside exclusively. For devices to be placed on the market, please refer to QP.03F[(102)].

5.7.1.1 Responsibility

M&H are to provide the expert supervisory overview of the development and design of the device, to ensure that the exemption requirements of the UK legislation relating to medical devices and in vitro diagnostic devices, are adhered to.

M&H are to ensure that devices meet the required standards and requirements of the relevant UK law.

M &H will require the appropriate staff to ensure that the design and development in relation to these devices follow the industry standard processes and procedures for medical and in vitro device development and manufacture production.

One point to note is the need to identify the senior staff who will be responsible for signing the declaration that the device meets the requirements of the exemptions.

5.7.1.2 Documentation to be produced

There will need to be a section detailing the documentation to be produced and how it will be reviewed to ensure it meets the exemption requirements. The following is a list of required documentation:

1. Details of how to identify the device,
2. Details of the manufacturing health institution
3. A statement of why the function of the device cannot be met by currently available devices on the market.
4. The intended purpose and performance of the device, how it functions, the user information, and how it is maintained and if necessary calibrated to ensure it is fit for use,
5. Details of how the device meets the relevant general safety and performance requirements and an explanation of those not applicable.
6. The manufacturing documentation and proof that the device is manufactured in accordance with these documents
7. Details of how the clinical use experience will be gathered, evaluated and acted upon.

This section will also detail how the documentation, and in particular, how all the elements of the 'Technical File' are to be retained. For work undertaken with academics the documentation may also include research theses. Details of these how these theses will be retained, and how to access the research associated with these theses will also need to be documentation. It must be emphasised that the theses will all need to be retained, and accessible for the lifetime of the device and possibly longer, depending on the type of device manufactured or produced.

5.7.1.3 Project control and review

This section will need to detail the areas relating to planning, device specification, review, hazard and risk analysis, validation and verification testing, transfer of design to manufacture and change control.

Appendix C5 6 is a draft copy of the proposed control documentation.

Chapter 6 CONCLUSIONS

The work undertaken throughout this thesis has successfully addressed the main aim, which was, to produce guidelines that would ensure that academics and third parties, collaborating with M&H meet the legislative and regulatory requirements for the development and manufacture of medical or in vitro diagnostic devices to be used 'in-house' within NHS Tayside.

It has been shown that, unless academics or third parties follow these guidelines, it will no longer be possible for them to manufacture such devices for use within health care institutions once the new UK legislation comes into force.

To achieve the aim detailed above, a comprehensive review of the medical and in vitro diagnostic device legislation coming into force within the EU and UK was undertaken. The result of this review highlighted the changes required by the M&H QMS in order to comply with the requirements of this legislation.

As detailed in the main body of this thesis, the development and manufacture of medical and in vitro diagnostic devices must adhere to an appropriate quality management system. The M&H accreditation to the BS EN ISO 13485 standard demonstrates that the work undertaken was controlled by such a quality management system. Significant work, as detailed within this thesis, was undertaken to maintain accreditation by achieving accreditation to the (BS EN ISO 13485:2016). Thus ensuring that the development of 'in-house' medical and in vitro diagnostic devices by M&H and those collaborating with M&H could continue.

By using information gained from the review of the medical and in vitro diagnostic device legislation, a comprehensive review of the University of Dundee OCE system was carried out to determine what modifications to the system were required to ensure that it was fit for use within a healthcare environment. Following this, the documentation to evidence that the OCE system met the exemption requirements, as detailed in the UK law for an 'in-house' manufactured in vitro diagnostic device, was identified. Draft copies of some of these documents are contained, and referred to within this thesis.

The continuation of this project is detailed in the following chapter.

Chapter 7 FURTHER WORK

The following points need to be addressed in the future:

In order to allow the UOD project work to continue to be used within a health care environment, the proposed guidelines need to be reviewed and issued by the appropriate staff of the University of Dundee. These issued guidelines then need to be incorporated into the relevant / appropriate student handbooks to ensure that the requirements, relating to the design and manufacture of devices and which might be used within a healthcare institution, are detailed.

It is necessary to continue developing the OCE system, and the associated documentation, to ensure that it meets the exemption requirements of the UK law to enable it to be used in the ongoing evaluation of this promising new diagnostic aid.

As a result of the UK leaving the EU, the UK government is reviewing the current medical and in vitro diagnostic device legislation. Part of the further work, arising from this thesis, would be to monitor any proposals to the current legislation so as to determine how it may affect the exemption requirements related to ‘in-house’ design and manufacture of medical and in vitro diagnostic devices.

Finally, as a result of the review of the medical and in vitro diagnostic device legislation and the work undertaken to gain accreditation to the latest revision of the BS EN ISO 13485 standard, a number of new quality documents have been proposed. This new documentation needs to be finalised and issued. Without these new quality documents, the accreditation will not be able to be maintained nor show that the department is compliant with the UK or EU legislation. Such inability to demonstrate compliance with the legislation or failure to maintain accreditation to BS EN ISO 13485, will significantly impact on the work to design and manufacture medical or in vitro diagnostic devices.

Chapter 8 **APPENDIX**

Appendix C3 1 Template Differences between ISO 13485:2003/2012 and ISO 13485 2016 with comments on changes and interpretation.

From https://elsmar.com/elsmarqualityforum/members/marmotte.50524

ISO 13485:2003, EN ISO 13485:2012	***ISO 13485:2016, EN ISO 13485:2016***	***Comments on change from ISO doc itself – Table A1***	***Personal interpretation /details / extracts***
	0.1 General	— Includes substantially more detail related to the nature of the organization covered by this International Standard's requirements and the life-cycle stages covered. — Explains that the requirements can be used by suppliers or other external parties either voluntarily or as a result of contract arrangements. — Alerts organizations about their obligations related to regulatory requirements focused on quality management systems. — Alerts organizations about differences in local regulation definitions and their obligation to understand how these definitions will affect their quality management system. — Adds the obligation to meet the organization's own quality management system requirements. — Specifically calls out the focus on the necessity to "meet customer and applicable regulatory requirements for safety and performance." — Emphasizes that the product requirements that are important are those related to safety and performance. — Adds two influences on the nature of the quality management system that were not in the original listing (organizational environment and regulatory requirements). — Clarifies that the organization does not have to align its documentation to the clause structure of this International Standard.	- No normative content; No impact.
	0.2 Clarification of concepts	— Adds two additional criteria associated with the description of appropriate requirements: — compliance with regulatory requirements;	- No normative content; No impact.

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
		— the requirement is necessary for the organization to manage risks. — Limits application of risk to the safety or performance requirements of the medical device or meeting applicable regulatory requirements. — Clarifies that the term “documented” includes the need to establish, implement and maintain. — Clarifies that the term “product” applies to outputs that are intended for, or required by, a customer, or any intended output resulting from a product realization process.	
	0.3 Process approach	Explanation of process approach extended.	- No normative content ; No impact.
	0.4 Relationship with ISO 9001	— States the relationship between ISO 13485:2016 and ISO 9001. — Indicates the structural relationship between ISO 13485:2016 and ISO 9001:2015 will be outlined in Annex B. — The use of italic text within standard to indicate changes from ISO 9001:2008 has been eliminated.	- No normative content ; No impact.
	1 Scope	— Indicates the applicability of this International Standard to organizations that are involved in one or more stages of the life-cycle of a medical device. — Indicates that this International Standard can also be used by suppliers or external parties that provide product, including quality management system-related services to medical device organizations. — Specifically calls out the responsibilities for monitoring, maintaining, and controlling outsourced processes. — Expands requirements that can be not applicable to those in Clauses 6 and 8. — Clarifies that the term “regulatory requirements” includes statutes, regulations, ordinances or directives and limits the scope of the “applicable regulatory requirements” to those requirements for the quality management system and the safety or performance of the medical device.	- No Direct impact.

ISO 13485:2003, EN ISO 13485:2012	***ISO 13485:2016, EN ISO 13485:2016***	***Comments on change from ISO doc itself – Table A1***	***Personal interpretation /details / extracts***
	3 Terms and definitions	— Several new definitions added and some existing definitions refined.	- No Direct impact.
4 Quality management system 4.1 General requirements	4 Quality management system 4.1 General requirements	— Added requirement to document the role(s) of the organization. — Requires the determination of processes "taking into account the roles undertaken by the organization." — Requires the application of a "risk based approach to the control of the appropriate processes needed for the quality management system." — Adds requirements related to changes to processes. — Added requirements related to validation of the application of computer software used in the quality management system.	4.1.1. The organization shall document the role(s) undertaken by the organization under the applicable regulatory requirements. NOTE Roles undertaken by the organization can include manufacturer, authorized representative, importeror distributor. 4.1.2. b) apply a risk based approach to the control of the appropriate processes needed for the quality management system; 4.1.4[...]Changes to be made to these processes shall be: a) evaluated for their impact on the quality management system; b) evaluated for their impact on the medical devices produced under this quality management system; c) controlled in accordance with the requirements of this International Standard and applicable regulatory requirements.

ISO 13485:2003, EN ISO 13485:2012	***ISO 13485:2016, EN ISO 13485:2016***	***Comments on change from ISO doc itself – Table A1***	***Personal interpretation /details / extracts***
			Also 4.1.5 "monitor outsourced processed" – e.g. consultant – require written agreement 4.1.6 SW validation + revalidation after change
4.2 Documentation requirements 4.2.1 General	4.2 Documentation requirements 4.2.1 General	- No Change	- No Change
4.2.2 Quality manual	4.2.2 Quality manual	- No Change	- No Change
4.2.3 Control of documents 4.2.4 Control of records	4.2.3 Medical device file 4.2.4 Control of documents 4.2.5 Control of records	Includes control of records within the document control requirements. Lists the documents that would be included in the medical device file. New requirement related to protection of confidential health information. New requirement related to deterioration and loss of documents	-
5 Management responsibility 5.1 Management commitment	5 Management responsibility 5.1 Management commitment	- No Change	- No Change
5.2 Customer focus	5.2 Customer focus	- No Change	- No Change
5.3 Quality policy	5.3 Quality policy	- No Change	- No Change
5.4 Planning 5.4.1 Quality objectives	5.4 Planning 5.4.1 Quality objectives	- No Change	- No Change

ISO 13485:2003, EN ISO 13485:2012	***ISO 13485:2016, EN ISO 13485:2016***	***Comments on change from ISO doc itself – Table A1***	***Personal interpretation /details / extracts***
5.4.2 Quality management system planning	5.4.2 Quality management system planning	- No Change	- No Change
5.5 Responsibility, authority and communication 5.5.1 Responsibility and authority	5.5 Responsibility, authority and communication 5.5.1 Responsibility and authority	- No Change	- No Change
5.5.2 Management representative	5.5.2 Management representative	- No Change	- No Change
5.5.3 Internal communication	5.5.3 Internal communication	- No Change	- No Change
5.6 Management review 5.6.1 General 5.6.2 Review input 5.6.3 Review output	5.6 Management review 5.6.1 General 5.6.2 Review input 5.6.3 Review output	— Includes requirement for the documentation of one or more procedures for management review and the requirement for management reviews at "documented planned intervals". — Lists of inputs and outputs of management review have been expanded.	Change from "management reviews at planned intervals" to "management reviews at documented planned intervals". Lists expansions are more details but no real new content
6. Resource management 6.1 Provision of resources	6. Resource management 6.1 Provision of resources	- No Change	- No Change
6.2 Human resources 6.2.1 General 6.2.2 Competence,	6.2 Human resources	— New requirement for documentation processes of establishing competence, providing needed training and ensuring awareness of personnel.	"The organization shall document the process(es) for establishing competence, providing needed training, and

ISO 13485:2003, EN ISO 13485:2012	***ISO 13485:2016, EN ISO 13485:2016***	***Comments on change from ISO doc itself – Table A1***	***Personal interpretation /details / extracts***
awareness and training			ensuring awareness of personnel"
6.3 Infrastructure	6.3 Infrastructure	- Adds requirement that infrastructure prevents product mix-up and ensure orderly handling of product. - Adds information system to the listing of supporting services.	- Besides of the two points on the left – there is now a requirement for the organization to DOCUMENT THE REQUIREMENTS.
6.4 Work environment	6.4 Work environment and contamination control 6.4.1 Work environment 6.4.2 Contamination control	- Added documentation requirements for work environment. — Added requirement related to control of contamination with microorganism or particulate matter for sterile medical devices.	- As above – new DOCUMENTAITON requirement
7 Product realization 7.1 Planning of product realization	7 Product realization 7.1 Planning of product realization	— Added requirements to list.	new c) "required [...]measurement [...], handling, storage, distribution and traceability [...]
7.2 Customer-related processes 7.2.1 Determination of requirements related to the product 7.2.2 Review of requirements related to the product	7.2 Customer-related processes 7.2.1 Determination of requirements related to the product 7.2.2 Review of requirements related to the product	- Added requirements to list :	- 7.2.1 "d) any user training needed to ensure specified performance and safe use of the medical device;" - 7.2.2. c) applicable regulatory requirements are met; - d) any user training identified in accordance with 7.2.1 is

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
			available or planned to be available;
7.2.3 Customer communication	7.2.3 Communication	— New requirement related to communication with regulatory authorities.	"The organization shall communicate with regulatory authorities in accordance with applicable regulatory requirements." Weird statement placement
7.3 Design and development 7.3.1 Design and development planning	7.3 Design and development 7.3.1 General 7.3.2 Design and development planning	- Added requirements to list. — Eliminated the requirement related to the management of the interfaces between different groups involved in design and development.	7.3.2 e) the methods to ensure traceability of design and development outputs to design and development inputs; - f) the resources needed, including necessary competence of personnel.
7.3.2 Design and development inputs	7.3.3 Design and development inputs	— Added requirements to list. — Added requirement that the requirements shall be able to be verified or validated.	- Added "usability" + ref to IEC62366
7.3.3 Design and development outputs	7.3.4 Design and development outputs	No Change	- No Change
7.3.4 Design and development review	7.3.5 Design and development review	Added details of the contents of records.	"include the - identification of the design under review, the participants involved and the date of the review"
7.3.5 Design and development verification	7.3.6 Design and development verification	Added requirement for documentation of verification plans and interface considerations. — Requirement added for records of verification.	New : "The organization shall document verification plans that

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
			include methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size. If the intended use requires that the medical device be connected to, or have an interface with, other medical device(s), verification shall include confirmation that the design outputs meet design inputs - when so connected or interfaced." Also added "Records of the - results AND CONCLUSIONS of […]"
7.3.6 Design and development validation	7.3.7 Design and development validation	— Added requirement for documentation of validation plans, product to be used for validation and interface considerations. Requirement added for records of validation.	New "The organization shall document validation plans that include methods, acceptance criteria and, as appropriate, statistical techniques with rationale for sample size." New "A medical device used for clinical evaluation or performance evaluation is not considered to be released for use to the customer. If the intended use requires that the medical

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
			device be connected to, or have an interface with, other medical device(s), validation shall include confirmation that the requirements for the specified application or intended use have been met when so connected or interfaced"
	7.3.8 Design transfer	New Sub-clause added	A medical device used for clinical evaluation or performance evaluation is not considered to be released for use to the customer. If the intended use requires that the medical device be connected to, or have an interface with, other medical device(s), validation shall include confirmation that the requirements for the specified - application or intended use have been met when so connected or interfaced
7.3.7 Control of design and development changes	7.3.9 Control of design and development changes	Adds the requirement that the evaluation of the change effect should be made on products in process and on the outputs of risk management and product realization processes — Added detail to consider in the determination of the significance of a design and development changes	New ":The organization shall determine the significance of the change to function, performance, usability, safety and applicable regulatory requirements for the medical device and its intended use."

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
			- Also note the "products in process and on the outputs of risk management and product realization processes" as opposed to only released products + records of "changes, THEIR REVIEW […]"
	7.3.10 Design and development files	— New sub-clause added.	- New but not really – i.e. DHF
7.4 Purchasing 7.4.1 Purchasing process	7.4 Purchasing 7.4.1 Purchasing process	— Focuses the supplier selection criteria on the effect of the supplier performance on the quality of the medical device, the risk associated with the medical device, and the product meeting applicable regulatory requirements. — New requirements added related to monitoring and re-evaluation of suppliers, and action to be taken when purchasing requirements are not met. — Provides addition details related to the content of the records.	- As explained
7.4.2 Purchasing information	7.4.2 Purchasing information	— New requirement added to include notification of changes in purchased product.	"Purchasing information shall include, as applicable, a written agreement that the supplier notify the organization of changes in the purchased product prior to implementation of any changes that affect - the ability of the purchased product to meet specified purchase requirements"
7.4.3 Verification of purchased product	7.4.3 Verification of purchased product	New requirements added on the extent of verification activities and action to be taken when the organization becomes aware of any changes to the purchased product.	Also new "The extent of verification activities shall be based on the supplier evaluation

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
			results and proportionate to the risks associated with the purchased product. When the organization becomes aware of any changes to the purchased product, the organization shall determine whether these changes affect the product realization process or the medical device."
7.5 Production and service provision 7.5.1 Control of production and service provision 7.5.1.1 General requirements	7.5 Production and service provision 7.5.1 Control of production and service provision	7.5.1 - Adds details related to the controls for carrying out production and service provision.	- Rewording but can't find anything really different ?
7.5.1.2 Control of production and service provision - Specific requirements 7.5.1.2.1 Cleanliness of product and contamination control	7.5.2 Cleanliness of product	7.5.2 - Added a requirement to the list.	- New c) product cannot be cleaned prior to sterilization or its use, and its cleanliness is of significance in use;

ISO 13485:2003, EN ISO 13485:2012	***ISO 13485:2016, EN ISO 13485:2016***	***Comments on change from ISO doc itself – Table A1***	***Personal interpretation /details / extracts***
7.5.1.2.2 Installation activities	7.5.3 Installation activities		- No Change
7.5.1.2.3 Servicing activities	7.5.4 Servicing activities	7.5.4 -— New requirement for analysis of records for servicing activities.	New "The organization shall analyse records of servicing activities carried out by the organization or its supplier: a) to determine if the information is to be handled as a complaint; - b) as appropriate, for input to the improvement process."
7.5.1.3 Particular requirements for sterile medical devices	7.5.5 Particular requirements for sterile medical devices		- No change
7.5.2 Validation of processes for production and service provision 7.5.2.1 General requirements	7.5.6 Validation of processes for production and service provision	-Added requirements to the list — Adds details related to situations requiring procedures. — Relates the specific approach to software validation to the risk associated with the use of the software. — Adds requirements related to the validation records.	- d) as appropriate, statistical techniques with rationale for sample sizes; - f/criteria for revalidation; - g) approval of changes to the processes. The specific approach and activities associated with software validation and revalidation shall be proportionate to the risk

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
			associated with the use of the software, including the effect on the ability of the product to conform to specifications. Record of [...]results and conclusion of validation and necessary actions[...]
7.5.2.2 Particular requirements for sterile medical devices	7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems	— Added requirements for sterile barrier systems.	- As explained
7.5.3 Identification and traceability 7.5.3.1 Identification	7.5.8 Identification	Added requirement for unique device identification. — New requirement for a documented procedure for product identification and regarding identification and product status during production	New "The organization shall identify product status with respect to monitoring and measurement requirements throughout product realization. Identification of product status shall be maintained throughout production, storage, installation and servicing of product to ensure that only product that has passed the required inspections and tests or released under an authorized concession is dispatched,used or installed.

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
			- If required by applicable regulatory requirements, the organization"
7.5.3.2 Traceability 7.5.3.2.1 General 7.5.3.2.2 Particular requirements for active implantable medical devices and implantable medical devices 7.5.3.3 Status identification	7.5.9 Traceability		- No Change
7.5.4 Customer property	7.5.10 Customer property		- No Change
7.5.5 Preservation of product	7.5.11 Preservation of product	Adds details as to how preservation can be accomplished.	The organization shall protect product from alteration, contamination or damage when exposed to expected conditions and hazards during processing, storage, handling, and distribution by: a) designing and constructing suitable packaging and shipping containers; b) documenting requirements for special conditions needed if

ISO 13485:2003, EN ISO 13485:2012	***ISO 13485:2016, EN ISO 13485:2016***	***Comments on change from ISO doc itself – Table A1***	***Personal interpretation /details / extracts***
			packaging alone cannot provide preservation
7.6 Control of monitoring and measuring devices	7.6 Control of monitoring and measuring equipment		- No change
8 Measurement, analysis and improvement 8.1 General	8 Measurement, analysis and improvement 8.1 General		- No Change
8.2 Monitoring and measurement 8.2.1 Feedback	8.2 Monitoring and measurement 8.2.1 Feedback	Indicates that feedback should come from production and post-production activities. — Adds a requirement to utilize feedback in risk management processes in order to monitor and maintain product requirements.	New The organization shall document procedures for the feedback process. This feedback process shall include provisions to gather data from production as well as post-production activities. The information gathered in the feedback process shall serve as potential input into risk management for monitoring and maintaining the product requirements as well as the product realization or improvement processes Note that link to CAPArs disappeared
	8.2.2 Complaint handling	— New sub-clause.	- New

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
	8.2.3 Reporting to regulatory authorities	— New sub-clause.	- New
8.2.2 Internal audit	8.2.4 Internal audit		- No change
8.2.3 Monitoring and measurement of processes	8.2.5 Monitoring and measurement of processes		- No Change -
8.2.4 Monitoring and measurement of product 8.2.4.1 General requirements 8.2.4.2 Particular requirement for active implantable medical devices and implantable medical devices	8.2.6 Monitoring and measurement of product	— Adds requirement to identify the test equipment used to perform measurement activities.	As appropriate, records shall identify the test equipment used to perform measurement activities.
8.3 Control of nonconforming product	8.3 Control of nonconforming product 8.3.1 General 8.3.2 Actions in response to nonconforming product detected before delivery 8.3.3 Actions in response to nonconforming	— Added details related to kinds of controls that shall be documented. — Generalized the requirement to include any investigation and the rationale for decisions. — Adds requirements related to concessions. — Separated requirements for nonconformities detected before delivery, detected after delivery and rework. — Adds requirements for records related to the issuance of advisory notices.	As explained

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments on change from ISO doc itself – Table A1*	*Personal interpretation /details / extracts*
	product detected after delivery 8.3.4 Rework		
8.4 Analysis of data	8.4 Analysis of data	Adds the requirement to include determination of appropriate methods, including statistical techniques and the extent of their use. — Adds detail to list of inputs.	Stats as explained + e) audits; f) service reports, as appropriate. If the analysis of data shows that the quality management system is not suitable, adequate or effective, - the organization shall use this analysis as input for improvement as required in 8.5.
8.5 Improvement 8.5.1 General	8.5 Improvement 8.5.1 General		- No change -
8.5.2 Corrective action	8.5.2 Corrective action	Adds the requirement to verify that the corrective action does not have an adverse effect. — Added requirement for corrective action to be taken without undue delay.	- As explained
8.5.3 Preventive action	8.5.3 Preventive action	- Adds the requirement to verify that the preventive action does not have an adverse effect.	- As explained

Appendix C3 2 Template Differences between ISO 13485:2003/2012 and ISO 13485 2016 with space for individual comments.

From https://elsmar.com/elsmarqualityforum/members/bjohnsonrli.278996/

ISO 13485:2003, EN ISO 13485:2012	*ISO 13485:2016, EN ISO 13485:2016*	*Comments*
4 Quality management system 4.1 General requirements	4 Quality management system 4.1 General requirements	
4.2 Documentation requirements 4.2.1 General	4.2 Documentation requirements 4.2.1 General	
4.2.2 Quality manual	4.2.2 Quality manual	
4.2.3 Control of documents 4.2.4 Control of records	4.2.3 Medical device file 4.2.4 Control of documents 4.2.5 Control of records	
5 Management responsibility 5.1 Management commitment	5 Management responsibility 5.1 Management commitment	
5.2 Customer focus	5.2 Customer focus	
5.3 Quality policy	5.3 Quality policy	
5.4 Planning 5.4.1 Quality objectives	5.4 Planning 5.4.1 Quality objectives	
5.4.2 Quality management system planning	5.4.2 Quality management system planning	
5.5 Responsibility, authority and communication 5.5.1 Responsibility and authority	5.5 Responsibility, authority and communication 5.5.1 Responsibility and authority	
5.5.2 Management representative	5.5.2 Management representative	
5.5.3 Internal communication	5.5.3 Internal communication	

5.6 Management review 5.6.1 General 5.6.2 Review input 5.6.3 Review output	5.6 Management review 5.6.1 General 5.6.2 Review input 5.6.3 Review output	
6. Resource management 6.1 Provision of resources	6. Resource management 6.1 Provision of resources	
6.2 Human resources 6.2.1 General 6.2.2 Competence, awareness and training	6.2 Human resources 6.2.1 General 6.2.2 Competence, awareness and training	
6.3 Infrastructure	6.3 Infrastructure	
6.4 Work environment	6.4 Work environment and contamination control 6.4.1 Work environment 6.4.2 Contamination control	
7 Product realization 7.1 Planning of product realization	7 Product realization 7.1 Planning of product realization	
7.2 Customer-related processes 7.2.1 Determination of requirements related to the product 7.2.2 Review of requirements related to the product 7.2.3 Customer communication	7.2 Customer-related processes 7.2.1 Determination of requirements related to the product 7.2.2 Review of requirements related to the product 7.2.3 Communication	
7.3 Design and development 7.3.1 Design and development planning	7.3 Design and development 7.3.1 General 7.3.2 Design and development planning	
7.3.2 Design and development inputs	7.3.3 Design and development inputs	

7.3.3 Design and development outputs	7.3.4 Design and development outputs	
7.3.4 Design and development review	7.3.5 Design and development review	
7.3.5 Design and development verification	7.3.6 Design and development verification	
7.3.6 Design and development validation	7.3.7 Design and development validation	
	7.3.8 Design transfer	
7.3.7 Control of design and development changes	7.3.9 Control of design and development changes	
	7.3.10 Design and development files	
7.4 Purchasing 7.4.1 Purchasing process	7.4 Purchasing 7.4.1 Purchasing process	
7.4.2 Purchasing information	7.4.2 Purchasing information	
7.4.3 Verification of purchased product	7.4.3 Verification of purchased product	
7.5 Production and service provision 7.5.1 Control of production and service provision 7.5.1.1 General requirements 7.5.1.2 Control of production and service provision - Specific requirements 7.5.1.2.1 Cleanliness of product and contamination control 7.5.1.2.2 Installation activities 7.5.1.2.3 Servicing activities 7.5.1.3 Particular requirements for sterile medical devices 7.5.2 Validation of processes for production and service provision 7.5.2.1 General requirements	7.5 Production and service provision 7.5.1 Control of production and service provision 7.5.2 Cleanliness of product 7.5.3 Installation activities 7.5.4 Servicing activities 7.5.5 Particular requirements for sterile medical devices 7.5.6 Validation of processes for production and service provision 7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems	

7.5.2.2 Particular requirements for sterile medical devices		
7.5.3 Identification and traceability 7.5.3.1 Identification 7.5.3.2 Traceability 7.5.3.2.1 General 7.5.3.2.2 Particular requirements for active implantable medical devices and implantable medical devices 7.5.3.3 Status identification	7.5.8 Identification 7.5.9 Traceability	
7.5.4 Customer property	7.5.10 Customer property	
7.5.5 Preservation of product	7.5.11 Preservation of product	
7.6 Control of monitoring and measuring devices	7.6 Control of monitoring and measuring equipment	
8 Measurement, analysis and improvement 8.1 General	8 Measurement, analysis and improvement 8.1 General	
8.2 Monitoring and measurement 8.2.1 Feedback	8.2 Monitoring and measurement 8.2.1 Feedback 8.2.2 Complaint handling	
	8.2.3 Reporting to regulatory authorities	
8.2.2 Internal audit	8.2.4 Internal audit	
8.2.3 Monitoring and measurement of processes	8.2.5 Monitoring and measurement of processes	
8.2.4 Monitoring and measurement of product 8.2.4.1 General requirements	8.2.6 Monitoring and measurement of product	

8.2.4.2 Particular requirement for active implantable medical devices and implantable medical devices		
8.3 Control of nonconforming product	8.3 Control of nonconforming product 8.3.1 General 8.3.2 Actions in response to nonconforming product detected before delivery 8.3.3 Actions in response to nonconforming product detected after delivery 8.3.4 Rework	
8.4 Analysis of data	8.4 Analysis of data	
8.5 Improvement 8.5.1 General	8.5 Improvement 8.5.1 General	
8.5.2 Corrective action 8.5.3 Preventive action	8.5.2 Corrective action 8.5.3 Preventive action	

Appendix C3 3 Completed BSI Readiness Review

Note Pictures in this appendix cropped to reduce document file size.

ISO 13485:2016 Readiness Review

Company name: Medical Physics & HMFUS
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C/O Dept of Medical Physics Ninewells Hospital and Medical School NHS Tayside Dundee DD1 9SY
Certification No.: MD 77843
Date: 23rd May 2017

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How ready are you for ISO 13485:2016?

BSI is committed to ensuring a smooth assessment for all clients wishing to certify to ISO 13485:2016, whether you are new to the standard or transitioning from ISO 13485:2003 / EN ISO 13485:2012.

This document allows you to detail how you intend to meet the additional requirements of the new standard, so should be used in conjunction with ISO 13485:2016. It is not an exhaustive checklist, but contains summary statements of most of the significant changes.

Completion of this form is not mandatory and does not need to form part of the transition process. However, you may find it a useful tool for analysing your progress prior to booking a transition assessment. Use the boxes below to list procedures, records and examples that address the additional requirements. This could be used as a gap analysis tool or as an aide memoire during your transition assessments.

If you have any questions during your journey please talk with you Client Manager or Assessor about your plans.

Clause 4 – Quality Management System

Clause 4.1 – General requirements

You will need to provide information on:

- Documenting the role of the organization;
- Awareness of the increased regulatory and risk based approach;
- Control of outsourced processes;
- Change management;
- Validation of software associated with the quality management system.

Role: section 1 (pg 3) QM
Regulatory / Risk: 2.2.3, 4.2.1, 5.1, 5.3, 5.5.1, 5.6.2, 6.2.2, 7.1, 7.3.2, 7.5.1
Outsourced: 7.3, 7.5.1 Management: 5.4, 5.6.2, 7.3.7, 7.5, 8.3
Validation: work required to define this, WI required

Clause 4.2 – Documentation requirements

You will need to provide information on:

- Non-application relating to clauses 6, 7 and 8;
- The medical device file;
- Additional controls related to document and record amendment, security and integrity, confidential health information.

Device File: 7.3, & QP.02 & associated WI's
Documentation: QP.01, QP.24 & section 4.2 in QM & associated WI's

Clause 5 – Management Responsibility

There are limited changes to this section, including:

- Increased focus on regulatory requirements;
- Documented procedures for management review; documented planned intervals; expanded inputs and outputs.

Management: Section 5 in the QM
Customer Focus: 5.2
Quality Policy: 5.3
Management Review: 5.6

Continued >>

Clause 6 – Resource Management

Clause 6.2 – Human resources

You will need to provide information on:

- Documented processes for competence, awareness and training;
- Risk based training effectiveness monitoring.

Human Resources including training & competence: 6.2 & QP.27

Clause 6.3 – Infrastructure

You will need to provide information on:

- Processes for preventing product mix-up;
- Information systems infrastructure;
- Maintenance intervals for production or monitoring equipment.

Infrastructure: 6.3

Clause 6.4 – Work environment

You will need to provide information on:

- Documentation requirements for work environment;
- Contamination controls for sterile medical devices.

Work Environment: 6.4 & QP.30
Contamination: 6.4.1

Clause 7 – Product Realization

Clause 7.1 – Planning of product realization

You will need to provide information on:

- Processes for risk management;
- Requirements for storage, handling, distribution and traceability.

Risk Management: 7.1, 7.3
Storage etc: 7.5 & QP.30, 03, 04, 02

Continued >>

Clause 7.2 – Customer related processes

You will need to provide information on:

- Requirement and availability for any user training;
- Documented processes for communicating with stakeholders, including regulatory authorities.

Training: 7.2 & QP.27
Communication: 7.2 & QP.02

Clause 7.3 – Design and development

You will need to provide information on:

- Traceability of design inputs to outputs;
- Required resources, including competence of personnel involved in design projects;
- Additional details and documentation for verification and validation plans, including statistical techniques, sampling rationale and representative product and records;
- Documented procedures for design transfer and design change;
- Design and development files.

Design & Development: 7.3 & QP.02 & associated WI's

Clause 7.4 – Purchasing

You will need to provide information on:

- Evidence of increased focus on supplier monitoring and risk;
- Documented agreements for prior notification of changes to supplied product;
- Linkage between verification of purchased product and change control.

Purchasing: 7.4 & QP.05

Continued >>

Clause 7.5 – Production and service provision

You will need to provide information on:

- Qualification of infrastructure;
- Analysis of service records;
- Documented procedures for validation including statistical techniques, sampling rationale, revalidation;
- Validation requirements for processes that cannot or are not subsequently monitored;
- Procedures for risk based software validation;
- Documented procedure for product identification/status during production; this may be Unique Device Identification (UDI), if required;
- Validation of sterile barrier systems;
- Suitability of packaging systems;
- Recording of measuring equipment adjustments.

Service Provision: 7.5

Clause 8 – Measurement, analysis and improvement

Clause 8.2 – Monitoring and measuring

You will need to provide information on:

- Linkages from customer feedback into risk management;
- Documented processes for ascertaining whether customer requirements have been met;
- Documented procedures for complaint handling;
- Communication processes for informing third parties of complaints;
- Documented plans for internal audits at defined intervals;
- Processes for the identification of test equipment.

Monitoring & Measuring: 8.2 & QP.35, QP.29, QP.26

Clause 8.3 – Control of non-conforming product

You will need to provide information on:

- Processes for communication with external parties regarding non-conforming product;
- Additional controls for managing concessions;
- Linkages between rework and regulatory requirements.

Non-conforming products: 8.3, QP.20

Continued >>

Clause 8.4 – Analysis of data

You will need to provide information on:

- Additional sources of data for analysis, such as service records and audits;
- Procedures that cover the application of statistical techniques;
- Linkages between the analysis and improvement processes.

Data: 8.4

Clause 8.5 – Improvement

You will need to provide information on:

- How actions are taken without undue delay;
- The evaluation of actions for adverse effects on regulatory requirements and product safety and performance.

Improvement: 8.5 & QP.20

Save

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Appendix C3 4 Full review of the present management system against the 13485:2016 standard. (QM issue 10)

For each clause and sub clause determine if the QM or relevant documents meet the requirements of the standard. If not indicate work to be undertaken.

Clause number and title	met yes/no,	If yes which document inc para number meets this need.	If no describe what needs to be added and to what document.	Change or new document implemented/date.
1 Scope	No		Not all the exclusions / clauses that are not applicable are noted in the QM scope. Also need to update various non 13485 scope entries.	QM SCOPE
2 Normative references	No		Need to update the 13485 year number also check other standards year numbers.	QM 3.1
3 Terms and definitions	No		Review the definitions especially for staff designations. Plus appendix 2 stuff	QM 3.2 and Appendix 2 and 3.

4 Quality management system				
4.1 General requirements	No		Missing the points 4.1.1 to 4.1.6	Need to possibly added the breakdown 4.1.1, to 4.1.6 to QM or something similar
4.1.1	No		Need to point to QM Introduction and Scope which details what each area does. Maybe expand the Instrumentation bit re medical device manufacture.	Review Introduction and Scope in QM
4.1.2	No		No mention of risk based approach as required by 13495:2016 in relevant areas. Plus point to the flowcharts and management stuff in appendix 2	Need to add risk based approached and review flowcharts appendix 5 and appendix 2.
4.1.3	No		Need to point to relevant areas of the QM which answer the points.	Review QM sections related to these points to ensure they meet these requirements audit and action forms, resources, objectives and KPI.
4.1.4	No		Again need to point to relevant areas of the QM which address these points.	Changes are planned and documented via Action forms QM planning and action form sections.

4.1.5	Yes	Subcontractors in purchasing and Supplier Performance -	Might be an idea to review supplier performance to ensure it meets these requirements	QP.11 not really QP.05
4.1.6	No		Software Validation	Get WI or SOP for this – needs to cover both purchased and 'in-house' software.

4.2 Documentation requirements	Yes			
4.2.1 General	YES	4.2.1 QM	Need to double check the list of QP verses 13485 clauses	Appendix 4
4.2.2 Quality manual	YES	4.2.2 QM	Need to double check the flowcharts of document and process interactions	Appendix 5
4.2.3 Medical device file	NO		Not got this at all.	Need to add 4.2.3
4.2.4 Control of documents	YES	4.2.3 QM and QP.01	Double check QP.01 has available for users as required and also printed doc legible. External docs as per point F. Plus G . The end point under point H review	QP.01 Possible change
4.2.5 Control of records	YES	4.2.4 and QP.24	Double check that 24 has legibility and retrievable.	QP.24 Possible change
5 Management responsibility				
5.1 Management commitment	YES	5.1		
5.2 Customer focus	NO Partial	5.2	Partially met. Does not state need to meet applicable regulatory requirements	Add to QM 5.2 about meeting stated and unstated regulatory needs

5.3 Quality policy	NO Partial	5.3	Partially met. Sections c and d need to check if these are mentioned in the policy.	Check QM 5.3 for the requirements of parts c) and d).
5.4 Planning				
5.4.1 Quality objectives	NO Partial	5.4.1	Review to ensure specifics relating to products are included	Review 5.4.1 required
5.4.2 Quality management system planning	NO Partial	5.4.2	Again review to ensure specifics related to products are included	Review 5.4.2 required
5.5 Responsibility, authority and communication				
5.5.1 Responsibility and authority	NO Partial	5.5.1 The word authority does not appear in this section	Need to amend this section to include staff authority	Need to review QM 5.5.1
5.5.2 Management representative	NO Partial	5.5.2 partially addresses this clause	Need to review and added in a few words to ensure section meets requriements	Review and amend 5.5.2
5.5.3 Internal communication	No		QM 5.5.3 does not actually state that the points in the standard will be met or how	Review 5.5.3
5.6 Management review				
5.6.1 General				
5.6.2 Review input	No Partial	Some in QM 5.6.2	QM 5.6.2 review for c) reporting to regulatory authorities; These mentioned but should they be better highlighted – split up in agenda??	QM 5.6.2 review for completeness

			e) monitoring and measurement of processes; f) monitoring and measurement of product; The following done but not specifically mentioned - g) corrective action; h) preventive action;	
5.6.3 Review output	No Partial	Some in 5.6.3	QM 5.6.3 the review minutes do not fully meet these requirements - are missing a) improvement needed to maintain the suitability, adequacy, and effectiveness of the quality management system and its processes; b) improvement of product related to customer requirements; c) changes needed to respond to applicable new or revised regulatory requirements;	Review to ensure these are noted in the minutes.

6 Resource management				
6.1 Provision of resources	NO Partial	QM 6.1 Part of a) and all of b)	QM 6.1 does it need to be modified or does it actually meet the statement a) a) implement the quality management system and to maintain its effectiveness;	
6.2 Human resources	NO Partial	QM 6.2 covers most aspects of the standard	QM 6.2 does not cover - The organization shall document the process(es) for establishing competence, providing needed training, and ensuring awareness of personnel. Nor NOTE The methodology used to check effectiveness is proportionate to the risk associated with the work for which the training or other action is being provided.	Qm 6.2 review and amend
6.3 Infrastructure	NO Partial	QM 6.3 Bits are ok	Not all aspects of 6.3 discussed in QM 6.3	QM 6.3 review and amend.
6.4 Work environment and contamination control	NO		QM 6.4 needs to be fully revised and rewritten.	QM 6.4
6.4.1 Work environment				
6.4.2 Contamination control				

7 Product realization	No Partial		Parts of the introduction are mixed up with the requirements of 7.1 and vice versa	Need to review Qm 7.1 and Qm 7 to unmix intro from clause 7.1 requriements
7.1 Planning of product realization	No Partial			Should this not point to qp.02 the project control procedure. Which should reiterate the relevant requirements of Section 7.
7.2 Customer-related processes	NO Partial			
7.2.1 Determination of requirements related to product	NO Partial		7.2.1 Points c) and d) missing.	Review QM 7.2.1 and add in these points
7.2.2 Review of requirements related to product	NO Partial		7.2.2 Points c) and d) missing and also the word documented is missing.	Review QM 7.2.2 and add in these points plus documented prior to commencement of work.
7.2.3 Communication	NO Partial		7.2.3 is point d) the same as standard 7.2.3 a). The note at the end of 7.2.3 is missing.	Review 7.2.3.

7.3 Design and development		Note that some of the QM heading change from 'Design and Development' to just 'design' or just 'Development'.	Need to keep heading the same please.	All QM section 7
7.3.1 General	Yes	Points to qp.02 but this 7.3.1 not actually in the QM	Review QP.02 to determine if all the points of clause 7 are included in it.	Review QP.02
7.3.2 Design and development planning	No Partial	This section QM 7.3.1 has all the requirements of 7.3.2 but not in same layout.	Review QM 7.3.1 to see if using the a), b) etc layout for the points would be better? This will change to 7.3.2 once added in the 7.3.1	Review Qm7.3.1
7.3.3 Design and development inputs	No Partial	This section QM 7.3.2 has all the requirements of 7.3.3 but not in same layout.	Review layout of QM 7.3.2. Also not all of the requirements of the last note in the clause seem to be in QM 7.3.2	Review QM 7.3.2
7.3.4 Design and development outputs	No Partial	Second sentence of 7.3.4 is not in QM 7.3.3.	Add the requirements of first note sentence of 7.3.4 plus wording at start of QM 7.3.3	Review QM 7.3.3.
7.3.5 Design and development review	No Partial	QM 7.3.4 covers the basics but not the full extent of the new standard 7.3.5	Review QM 7.3.4 to include all of the requirements	Review QM 7.3.4
7.3.6 Design and development verification	No Partial	QM 7.3.5 does not cover this fully	Review QM7.3.5 to ensure it meets the requirements of 7.3.6 of the standard.	Review QM 7.3.5
7.3.7 Design and development validation	NO		Review QM7.3.6 and amend as it does not cover 7.3.7 of the standard	Full review of QM 7.3.6 if required add to QP.02.

7.3.8 Design and development transfer	NO		This section does not exist in the QM. Add to QM	Additional section to QM
7.3.9 Control of design and development changes	No Partial	We have QP.20 but this not go into design change in any depth	Review QM 7.3.7 and amend to include all of the requirements of the standard 7.3.9	Full review of QM 7.3.7 if required add to QP.02.
7.3.10 Design and development files	NO		This section does not exist in the QM. Add to QM	Additional section to QM

7.4 Purchasing				
7.4.1 Purchasing process	No Partial	Qm7.4.1 does not full address this clause	No need to review risks. Also QM does not point to QP.11 or QP.20 or action forms	Review QM 7.4.1 against standard.
7.4.2 Purchasing information	No Partial		Point c) missing and need to define traceability better.	Review QM 7.4.2 and QP.05 (newest) agains standard.
7.4.3 Verification of purchased product	No Partial	It is all there apart from the last sentence of the clause.	No mention of documentation of certification activities. Might also be an idea to point to QP.05	QM 7.4.3

7.5 Production and service provision	No Partial	This whole section needs to be reviewed. Number of new requirements added and need to be addressed in the QM	Review all and amend as required	
7.5.1 Control of production and service provision			Has parts from the new sections mixed into it.	
7.5.2 Cleanliness of product	No		New section but look in old QM 7.5.1	
7.5.3 Installation activities	No		Not applicable do not do this	
7.5.4 Servicing activities	No		Need new section and fully detaile.	
7.5.5 Particular requirements for sterile medical devices	No		Needs a section	
7.5.6 Validation of processes for production and service provision	No partial		Was in QM 7.5.2 and needs new section with correct controls	
7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems	No		Not applicable but should point to accredited services	
7.5.8 Identification	No		This needs new section old QM 7.5.3 but mixed with new 7.5.9	
7.5.9 Traceability	No Partial		Have it but mixed with new 7.5.8	
7.5.10 Customer property	No Partial		Have it but needs reviewed against standard. We do not mention what to do if anything is wrong with the items	

			passed to us – this could be samples, material for a job, etc.	
7.5.11 Preservation of product	No Partial		Have it but needs reviewed against standard. Does not really detail product packaging.	
7.6 Control of monitoring and measuring equipment	No Partial		Have it but needs reviewed against standard – e.g. software validation	

8 Measurement, analysis and improvement				
8.1 General	NO Partial		QM 8.1 covers most of this clause but the word product is not really mentioned. Also need to add in changes to regulatory or relevant standards	
8.2 Monitoring and measurement	No Partial		8.2 in QM is one section covering all of 8.2.1, 8.2.2 and 8.2.3 in one lump. Maybe best to split it up and also add in the references to the various QPs also need to highlight QP names not complaint handling but customer feedback.	
8.2.1 Feedback			See 8.2	
8.2.2 Complaint handling			See 8.2	
8.2.3 Reporting to regulatory authorities			See 8.2	
8.2.4 Internal audit	No Partial		Some of the key words are missing from 8.2.2. For example planned, reviewed in light of precious findings and relevant to importance of activities.	
8.2.5 Monitoring and measurement of processes	YES but		Might be an idea to point to things like NSD contracts with indicators and objectives. Also M&H general objectives.	

8.2.6 Monitoring and measurement of product	No Partial		QM 8.2.4 no mention of sign off for product release. Could be e-quip job closed or as in SCPS sign off for patient report.	
8.3 Control of nonconforming product	No Partial		This is lumped in to 8.3 in the QM . Might be an idea to split up and also to point out that product includes test reports, completed repairs, patient treatment and etc.	
8.3.1 General			See 8.3	
8.3.2 Actions in response to nonconforming product detected before delivery			See 8.3	
8.3.3 Actions in response to nonconforming product detected after delivery			See 8.3	
8.3.4 Rework			See 8.3	
8.4 Analysis of data	NO Patrial		Need to review 8.4 Qm against the standard and also areas such as SCPS do use statistics to monitor their test results so need to add this in. Also no mention of audits or trending of AFs stc.	
8.5 Improvement				
8.5.1 General	YES but		Need to expand 8.1 QM to include the notion that training, audit and action	

			form findings are part of preventative actions.	
8.5.2 Corrective action	No Partial		Does answer the clause but could do better expecially in lloking at points a to f. This would also make things better for the other standards	
8.5.3 Preventive action	No Partial		No mention of embedded preventative actions – training competency auditing etc. It mainly looks at things that have been pointed out not that are in place to stop these things from happening, Also any need to do the breakdown of a to e?	

Appendix C3 5 Recommended changes to issue 10 of Quality Manual

Please note that the document given in this appendix was written for use by M&H quality staff. IT is given in this thesis for completeness. It is reproduced in full without amendments.

The procedure QP.03F was written to cover the specific requirements of the medical design and product standard 13485:2016 not correctly or fully included in Issue 10 Rev 0 of the M&H quality manual (The 2019 issue of this manual).

This was achieved by reviewing each clause of 13485, determining how M&H would meet the requirement or requirements of each 13485 clause, and if these requirements were met in the M&H quality manual, if not what additional requirements would need to be stated in the new procedure being written. On occasion, the 13485 requirement were addressed in the M&H quality manual but in a manner not fully directed at the requirements of the 13485 standard. For example Section 8 of the M&H manual covers corrective and preventative action in depth but the actions detailed are not specific enough to the 13485 standard.

The following details the gaps and required actions to ensure that the next issue of the M&H quality manual, Issue 11 Rev 0, better meets the requirements not just of the 13485 standard but the other standards M&H are certified or accredited to – 9001, 17025 and 15189.

General Changes:

The name of Medical Physics Instrumentation has been change to Clinical Engineer. Update manual to reflect this change and also better define the work of this group in the introduction and scope sections.

Review procedures referenced in the quality manual as some have had their title changed to better reflect the work or processes they control, some have been removed and a few new procedures, including QP.03F have been introduced.

SCPS should have its own paragraph in scope?

HMFUS are now part of Genetics – need to update this is rest of manual and also who they now report to.

The introduction to the quality manual, senior staff responsibility and organisation chart requires amended to ensure the changes to SCPS, HMFUS and Clinical Engineering management structures are included.

Changes to specific Clauses.

1 Introduction

SCPS and UKCAL laboratory functions need more visability – maybe break the Photobiology paragraph into sub heading.

Do same for Clinical Engineering.

2. Scope

2.2.4. No reference to HMFUS R&D work is against 13485 and 15189. Need to reference new MDR, IVDR and UK statue.

3. References and Definitions

Section 3.1 and 3.2 need review plus additions of documentation and corrective and add in some definitions for example preventative actions, risk review, avoidance and acceptable risk.

4. Quality Management System for M&H, NHS Tayside

4.1.2, 4.1.3 and 4.1.4 in 13485 should be addressed in QM as it will be of benefit to rest of system –

1. Risk based approached to the procedures and process and ensure appropriate interaction.
2. Review procedures and process are achievable with the resources available.
3. Planning to achieve required results and maintain effectiveness.
4. Reviewing document changes to ensure the changes do not adversely affect or interfere with other parts of the quality management system.

4.2 Documentation Requirements

More required as to the control of documentation given to or received from subcontractors. Needs to go into QP.01 – identification and control.

E-Quip and Q-Pulse location sharing not in QP.01 plus control of external manuals for change control or review – they are not under our control so can only ask for staff to check they are the correct issue for the job.

4.2.1 The management tree needs a review and update as mention of for example deputy quality manager role.

4.2.2 Review this section as some of it seems redundant – e,g, is Appendix 1 needed, The interaction appendix needs updated - new and removed documents.

Missing - No mention of special documentation as required by regulatory or statutory requirements. Could be a new section?

No mention of how subcontractors fit into the quality management system.

4.2.3 No mention of change control and how this achieved. Also check QP.01 to determine if change control detailed fully.

There is no mention of the control of documentation passed to or passed from subcontractors – check also QP.01 as to how subcontractors documentation (to or from) fits into our system. What about QP.24 for record retention in relation to subcontractors?

4.2.4 No longer have QP.03 remove reference.

4.4 Software Validation

Beef up to meet 4.1.6 and double check qp.01 against 4.1.6

5. Management Responsibility

5.1 Management Commitment

5.1 Review list order as a bit haphazard. Plus check the content – e,g, point g) seems ambiguous

5.2 Customer Focus

5.2 First list is missing the requirement to ensure we meet the needs of applicable regulatory or statutory requirements

5.3 M&H Quality Policy

5.3. The policy does not state that is communicated to staff nor reviewed for effectiveness.

Also might it be an idea to detail the requirements of a policy statement.

5.5 Responsibility, Authority and Communication

5.5.1 Need to review sentence two of 13485 5.5.1 – 'Top management shall document the interrelation of all personnel who manage, perform and verify work affecting quality and shall ensure the independence and authority necessary to perform these tasks.' As the QM really does not do this and it is required for 17025 and 15189.

5.5.2 Need to add in statutory …. In fact review all QM to have 'regulatory and statutory requirements'.

5.6 Management Review

5.6.2 Need to add in reporting to regulatory or statutory authorities to agenda.

Need to look at point 3 of agenda to possibly add in how the complaint was dealt with – complaint handling….

5.6.3 It might be beneficial to include the requirements of the 13485 review minutes into this section of the quality manual.

Also no mention of using action forms to recorded output of the reviews – things to be done or things to inform staff of – the good things and the not so good things….

6. Resource Management

6.1 Provisions of Resurces

There is no mention in the introduction regarding the need to have sufficient and correct resources to implement the QMS and maintain its effectiveness.

6.2 Human Resources

6.2.2 Nothing about reviewing the risk re training – is trained, competency and ability of staff reviewed against the risk of failing to carry out a task or fulfilling an output.

6.3 Infrastructure

Need to review this against the needs of 13285 to see if adding any of the ideas contained would be of benefits to the quality system.

6.4 Work Environment

6.4 change titles to included contamination control as it is required by 15189 and have new 6.4.1 and 6.4.2 paragraphs as per 13485.

7. Product & Service Provision

Sections 7.1, 7.2, 7.3 and 7.4 is now contained in new QP.03F for work related to medical devices, patient tests and associated services. Need to add into 7.3 design transfer documentation into quality manual as it would seem sensible to detail how the handover of the results of general design and development work documentation and information to be manufactured is achieved.

7.4 Purchasing

7.4.2 There is no mention of regulatory or statutory requirements nor the quality of the required products.

7.5 Production of Service Provision

7.5.1 Missing SCPS and Clinical Areas. Also how much of the Clinical Engineering section have changed due to the introduction of e-Quip.

7.5.3 Identification and traceability needs to be reviewed for need, in light of e-Quip and the need of the various standards.

7.5.4 Might be an idea to add in how customer supplied materials for incorporating into products are to be controlled.

7.5.5 Review this section against the requirements of 13458 7.5.11 for non-medical production work.

13485 Clause 7.5.7 needs to be reference in the quality manual to state that only approved external sterilisation processes.

7.6 Control of Monitoring and Measuring Devices

First sentence needs review as some parts do not seem to be correct.

Also need to look at

1. Ensure monitoring or calibrated equipment not inadvertently adjusted.
2. Having calibration results, external or internal, document as found results.
3. If monitoring or calibrated equipment is found to be in error or needs adjusted during calibration then need to determine how this error or adjustment has affected previous work and if rework or recall is required,

8 Measurement, analysis and improvement

8.2.1 Customer Satisfaction

Should this section not mention complaint handling?

8.3 Control of Non-Conformities

Seems to be missing section number 8.3.1for this General Section. Also the general section does not mention the need to involve subcontractors in the investigation and control of non-conformities their work / product / materials involved in.

Need to rectify other section numbering once 8.3.1 added.

8.4 Analysis of Data

The general outline of this section is not correct as SCPS have complex analysis of test result information – need to review this against 15189 and 17025 and 13485 as each of these standards have requirements for statistical analysis of data.

Appendix C4 1 The EU and UK Exemption Requirements for 'In-House' Manufacture

EU MDR[(2)]

Article 5

Placing on the market and putting into service

1. A device may be placed on the market or put into service only if it complies with this Regulation when duly supplied and properly installed, maintained and used in accordance with its intended purpose.
2. A device shall meet the general safety and performance requirements set out in Annex I which apply to it, taking into account its intended purpose.
3. Demonstration of conformity with the general safety and performance requirements shall include a clinical evaluation in accordance with Article 61.
4. Devices that are manufactured and used within health institutions shall be considered as having been put into service.
5. With the exception of the relevant general safety and performance requirements set out in Annex I, the requirements of this Regulation shall not apply to devices, manufactured and used only within health institutions established in the Union, provided that all of the following conditions are met:
    a) the devices are not transferred to another legal entity,
    b) manufacture and use of the devices occur under appropriate quality management systems,
    c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance by an equivalent device available on the market,
    d) the health institution provides information upon request on the use of such devices to its competent authority, which shall include a justification of their manufacturing, modification and use;
    e) the health institution draws up a declaration which it shall make publicly available, including:
        I) the name and address of the manufacturing health institution;
        II) the details necessary to identify the devices;
        III) a declaration that the devices meet the general safety and performance requirements set out in Annex I to this Regulation and, where applicable, information on which requirements are not fully met with a reasoned justification therefor,
    f) the health institution draws up documentation that makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and that is sufficiently detailed to enable the

competent authority to ascertain that the general safety and performance requirements set out in Annex I to this Regulation are met;

g) the health institution takes all necessary measures to ensure that all devices are manufactured in accordance with the documentation referred to in point (f), and

h) the health institution reviews experience gained from clinical use of the devices and takes all necessary corrective actions.

Member States may require that such health institutions submit to the competent authority any further relevant information about such devices which have been manufactured and used on their territory. Member States shall retain the right to restrict the manufacture and the use of any specific type of such devices and shall be permitted access to inspect the activities of the health institutions. This paragraph shall not apply to devices that are manufactured on an industrial scale.

6. In order to ensure the uniform application of Annex I, the Commission may adopt implementing acts to the extent necessary to resolve issues of divergent interpretation and of practical application. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 114(3).

EU IVDR[3]

Article 5

Placing on the market and putting into service

1. A device may be placed on the market or put into service only if it complies with this Regulation when duly supplied and properly installed, maintained and used in accordance with its intended purpose.
2. A device shall meet the general safety and performance requirements set out in Annex I which apply to it, taking into account its intended purpose.
3. Demonstration of conformity with the general safety and performance requirements shall include a clinical evaluation in accordance with Article 61.
4. Devices that are manufactured and used within health institutions shall be considered as having been put into service.
5. With the exception of the relevant general safety and performance requirements set out in Annex I, the requirements of this Regulation shall not apply to devices, manufactured and used only within health institutions established in the Union, provided that all of the following conditions are met:
   a) the devices are not transferred to another legal entity,
   b) manufacture and use of the devices occur under appropriate quality management systems,
   c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance by an equivalent device available on the market,
   d) the health institution provides information upon request on the use of such devices to its competent authority, which shall include a justification of their manufacturing, modification and use;
   e) the health institution draws up a declaration which it shall make publicly available, including:
      I) the name and address of the manufacturing health institution;
      II) the details necessary to identify the devices;
      III) a declaration that the devices meet the general safety and performance requirements set out in Annex I to this Regulation and, where applicable, information on which requirements are not fully met with a reasoned justification therefor,
   f) the health institution draws up documentation that makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and that is sufficiently detailed to enable the competent authority to ascertain that the general safety and performance requirements set out in Annex I to this Regulation are met;

g) the health institution takes all necessary measures to ensure that all devices are manufactured in accordance with the documentation referred to in point (f), and
h) the health institution reviews experience gained from clinical use of the devices and takes all necessary corrective actions.

Member States may require that such health institutions submit to the competent authority any further relevant information about such devices which have been manufactured and used on their territory. Member States shall retain the right to restrict the manufacture and the use of any specific type of such devices and shall be permitted access to inspect the activities of the health institutions.

This paragraph shall not apply to devices that are manufactured on an industrial scale.

6. In order to ensure the uniform application of Annex I, the Commission may adopt implementing acts to the extent necessary to resolve issues of divergent interpretation and of practical application. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 114(3).

UK Law [(4)]

Placing on the market and putting into service

71.—

1. A device to which this Part applies may be placed on the market or put into service only if it complies with this Part when duly supplied and properly installed, maintained and used in accordance with its intended purpose.
2. A device to which this Part applies must meet the general safety and performance requirements set out in Schedule 3 which apply to it, taking into account its intended purpose.
3. Demonstration of the general safety and performance requirements must include a clinical evaluation in accordance with regulation 102.
4. Devices that are manufactured and used within health institutions must be considered as having been put into service.
5. With the exception of the relevant safety and performance requirements set out in Schedule 3, the requirements of this Part do not apply to a device which is manufactured and used only within health institutions provided that—
    a) the device is not transferred to another legal entity;
    b) manufacture and use of the device occurs under appropriate quality management systems;
    c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance, by an equivalent device available on the market;
    d) on request from the Secretary of State, the health institution provides the Secretary of State with information (which must include justification for its manufacturing, modification and use of such devices) on the use of the devices;
    e) the health institution draws up and makes publically available a statement setting out—
        I) the name and address of the manufacturing health institution,
        II) the details necessary to identify the devices,
        III) a declaration that the devices meet the general safety and performance requirements set out in Schedule 3 or, where applicable, information on which requirements are not fully met and a reasoned justification for not meeting those requirements;
    f) the health institution draws up a document which makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices and the intended purpose, and which is sufficiently detailed to enable the Secretary of State to ascertain whether the general safety and performance requirements set out in Schedule 3 are met;

g) the health institution takes all necessary measures to ensure that the device is manufactured in accordance with the documentation referred to in sub-paragraph (f);

h) the health institution reviews experience gained from the clinical use of the devices and takes all necessary corrective actions.

6. The Secretary of State may require a health institution which has complied with paragraph (5) to provide the Secretary of State with any further information about the devices which it has manufactured or used.
7. The Secretary of State may restrict the manufacture and the use of a specified type of device manufactured in accordance with paragraph (5) and, for the purpose of considering such a restriction, must be permitted access to inspect the activities of health institutions.
8. Paragraph (5) does not apply to devices that are manufactured on an industrial scale.

Appendix C4 2 Side by side comparison of the exemption rules.

MDR -Article 5 Placing on the market and putting into service	IVDR Article 5 Placing on the market and putting into service	UK Para 71 Placing on the market and putting into service
1. A device may be placed on the market or put into service only if it complies with this Regulation when duly supplied and properly installed, maintained and used in accordance with its intended purpose.	1. A device may be placed on the market or put into service only if it complies with this Regulation when duly supplied and properly installed, maintained and used in accordance with its intended purpose.	1. A device to which this Part applies may be placed on the market or put into service only if it complies with this Part when duly supplied and properly installed, maintained and used in accordance with its intended purpose.
2. A device shall meet the general safety and performance requirements set out in Annex I which apply to it, taking into account its intended purpose.	2. A device shall meet the general safety and performance requirements set out in Annex I which apply to it, taking into account its intended purpose.	2. A device to which this Part applies must meet the general safety and performance requirements set out in Schedule 3 which apply to it, taking into account its intended purpose.
3. Demonstration of conformity with the general safety and performance requirements shall include a clinical evaluation in accordance with Article 61.	3. Demonstration of conformity with the general safety and performance requirements shall include a clinical evaluation in accordance with Article 61.	3. Demonstration of the general safety and performance requirements must include a clinical evaluation in accordance with regulation 102.
4. Devices that are manufactured and used within health institutions shall be considered as having been put into service.	4. Devices that are manufactured and used within health institutions shall be considered as having been put into service.	4. Devices that are manufactured and used within health institutions must be considered as having been put into service.

5. With the exception of the relevant general safety and performance requirements set out in Annex I, the requirements of this Regulation shall not apply to devices, manufactured and used only within health institutions established in the Union, provided that all of the following conditions are met: a) the devices are not transferred to another legal entity, b) manufacture and use of the devices occur under appropriate quality management systems, c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance by an equivalent device available on the market, d) the health institution provides information upon request on the use of such devices to its competent authority, which shall include a justification of their	5. With the exception of the relevant general safety and performance requirements set out in Annex I, the requirements of this Regulation shall not apply to devices, manufactured and used only within health institutions established in the Union, provided that all of the following conditions are met: a) the devices are not transferred to another legal entity, b) manufacture and use of the devices occur under appropriate quality management systems, c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance by an equivalent device available on the market, d) the health institution provides information upon request on the use of such devices to its competent authority, which shall include a justification of their	5. With the exception of the relevant safety and performance requirements set out in Schedule 3, the requirements of this Part do not apply to a device which is manufactured and used only within health institutions provided that— a) the device is not transferred to another legal entity; b) manufacture and use of the device occurs under appropriate quality management systems; c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance, by an equivalent device available on the market; d) on request from the Secretary of State, the health institution provides the Secretary of State with information (which must include justification for its manufacturing, modification and use of such devices) on the use of the devices;

manufacturing, modification and use;	manufacturing, modification and use;	e) the health institution draws up and makes publically available a statement setting out—
e) the health institution draws up a declaration which it shall make publicly available, including:	e) the health institution draws up a declaration which it shall make publicly available, including:	I) the name and address of the manufacturing health institution,
I) the name and address of the manufacturing health institution;	I) the name and address of the manufacturing health institution;	II) the details necessary to identify the devices,
II) the details necessary to identify the devices;	II) the details necessary to identify the devices;	III) a declaration that the devices meet the general safety and performance requirements set out in Schedule 3 or, where applicable, information on which requirements are not fully met and a reasoned justification for not meeting those requirements;
III) a declaration that the devices meet the general safety and performance requirements set out in Annex I to this Regulation and, where applicable, information on which requirements are not fully met with a reasoned justification therefor,	III) a declaration that the devices meet the general safety and performance requirements set out in Annex I to this Regulation and, where applicable, information on which requirements are not fully met with a reasoned justification therefor,	f) the health institution draws up a document which makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices and the intended purpose, and which is sufficiently detailed to enable the Secretary of State to ascertain whether the general safety and performance requirements set out in Schedule 3 are met;
f) the health institution draws up documentation that makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and that is sufficiently detailed to enable the competent authority to ascertain that the	f) the health institution draws up documentation that makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and that is sufficiently detailed to enable the competent authority to ascertain that the	

general safety and performance requirements set out in Annex I to this Regulation are met; g) the health institution takes all necessary measures to ensure that all devices are manufactured in accordance with the documentation referred to in point (f), and h) the health institution reviews experience gained from clinical use of the devices and takes all necessary corrective actions. Member States may require that such health institutions submit to the competent authority any further relevant information about such devices which have been manufactured and used on their territory. Member States shall retain the right to restrict the manufacture and the use of any specific type of such devices and shall be permitted access to inspect the activities of the health institutions.	general safety and performance requirements set out in Annex I to this Regulation are met; g) the health institution takes all necessary measures to ensure that all devices are manufactured in accordance with the documentation referred to in point (f), and h) the health institution reviews experience gained from clinical use of the devices and takes all necessary corrective actions. Member States may require that such health institutions submit to the competent authority any further relevant information about such devices which have been manufactured and used on their territory. Member States shall retain the right to restrict the manufacture and the use of any specific type of such devices and shall be permitted access to inspect the activities of the health institutions.	g) the health institution takes all necessary measures to ensure that the device is manufactured in accordance with the documentation referred to in sub-paragraph (f); h) the health institution reviews experience gained from the clinical use of the devices and takes all necessary corrective actions. 6. The Secretary of State may require a health institution which has complied with paragraph (5) to provide the Secretary of State with any further information about the devices which it has manufactured or used. 7. The Secretary of State may restrict the manufacture and the use of a specified type of device manufactured in accordance with paragraph (5) and, for the purpose of considering such a restriction, must be permitted access to inspect the activities of health institutions. 8. Paragraph (5) does not apply to devices that are manufactured on an industrial scale.

This paragraph shall not apply to devices that are manufactured on an industrial scale. **6.** In order to ensure the uniform application of Annex I, the Commission may adopt implementing acts to the extent necessary to resolve issues of divergent interpretation and of practical application. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 114(3).	This paragraph shall not apply to devices that are manufactured on an industrial scale. **6.** In order to ensure the uniform application of Annex I, the Commission may adopt implementing acts to the extent necessary to resolve issues of divergent interpretation and of practical application. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 114(3).	

Appendix C4 3 Comparison: Medical Devices EU with UK General Safety and Performance Requirements.

Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC, referenced as EU MDR		2019 No. 791 EXITING THE EUROPEAN UNION CONSUMER PROTECTION The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 Made - 1st April 2019
ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS	Comparison Yes /NO	Schedule 3 parts 1,2 and 3. General safety and performance requirements for general medical devices

CHAPTER I GENERAL REQUIREMENTS		PART 1 General requirements
1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be		1. Devices must— (a) achieve the performance intended by their manufacturer; (b) be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose; (c) be safe and effective and not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.

associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.		
2.The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.		2. The requirement in this Schedule to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.

3.Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall: (a) establish and document a risk management plan for each device; (b)identify and analyse the known and foreseeable hazards associated with each device; (c)estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d)eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4; (e)evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; and		3 - (1) Manufacturers must establish, implement, document and maintain a risk management system. (2) Risk management is to be understood as a continuous iterative process throughout the entire lifecycle of a device, which requires regular systematic updating and, in carrying out risk management, manufacturers must— (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in sub-paragraph (c) in accordance with the requirements of paragraph 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; (f) based on the evaluation of the impact of the information referred to in paragraph (e), if necessary amend control measures in line with the requirements of paragraph 4.

(f)based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.		

4.Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, Manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority: (a)eliminate or reduce risks as far as possible through safe design and manufacture; (b)where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c)provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users. Manufacturers shall inform users of any residual risks.		4 - (1) Risk control measures adopted by manufacturers for the design and manufacture of the devices must conform to safety principles, taking account of the generally acknowledged state of the art. (2) To reduce risks, manufacturers must manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. (3) In selecting the most appropriate solutions, manufacturers must, in the following order of priority— (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety (warnings, precautions, contra-indications) and, where appropriate, training to users; (d) inform users of any residual risks.

5.In eliminating or reducing risks related to use error, the manufacturer shall: (a)reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and (b)give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).	Page **201** of **513**	5. In eliminating or reducing risks related to use error, the manufacturer must— (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety); (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).
6.The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.		6. The characteristics and performance of a device must not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.
7.Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.		7. Devices must be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.

8.All known and foreseeable risks, and any undesirable side-effects, shall be minimised and be acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use.		8. All known and foreseeable risks, and any undesirable side-effects, must be minimised and be acceptable when weighed against the evaluated benefits to the patient or user arising from the achieved performance of the device during normal conditions of use.

9.For the devices referred to in Annex XVI, the general safety requirements set out in Sections 1 and 8 shall be understood to mean that the device, when used under the conditions and for the purposes intended, does not present a risk at all or presents a risk that is no more than the maximum acceptable risk related to the product's use which is consistent with a high level of protection for the safety and health of persons.		9. For the devices referred to in Schedule 16, the general safety requirements set out in paragraphs 1 and 8 must be understood to mean that the device, when used under the conditions and for the purposes intended, does not present a risk at all or presents a risk that is no more than the maximum acceptable risk related to the product’s use which is consistent with a high level of protection for the safety and health of persons.

The information and requirements in this section need to be reviewed each time EU or UK legislation change as section 10.4 is liable to change. The changes may not be reflected between the two sets of requirements.

CHAPTER II REQUIREMENTS REGARDING DESIGN AND MANUFACTURE		PART 2 Requirements regarding design and manufacture
Essential Requirement 10. Chemical, physical and biological properties		Chemical, physical and biological properties
10.1Devices shall be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Chapter I are fulfilled. Particular attention shall be paid to: (a)the choice of materials and substances used, particularly as regards toxicity and, where relevant, flammability; (b)the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant, absorption, distribution, metabolism and excretion; (c)the compatibility between the different parts of a device which consists of more than one implantable part; (d) the impact of processes on material properties;		10 .—(1) Devices must be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in paragraphs 1 to 9 are fulfilled. (2) Particular attention must be paid to— (a) the choice of materials and substances used, particularly as regards toxicity and, where relevant, flammability; (b) the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant, absorption, distribution, metabolism and excretion; (c) the compatibility between the different parts of a device which consists of more than one implantable part; (d) the impact of processes on material properties; (e) where appropriate, the results of biophysical or modelling research the validity of which has been demonstrated beforehand; (f) the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance and fatigue resistance;

(e)where appropriate, the results of biophysical or modelling research the validity of which has been demonstrated beforehand; (f)the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance and fatigue resistance; (g) surface properties; and (h)the confirmation that the device meets any defined chemical and/or physical specifications.		(g) surface properties; (h) the confirmation that the device meets any defined chemical or physical specifications.

10.2.Devices shall be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to patients, taking account of the intended purpose of the device, and to the persons involved in the transport, storage and use of the devices. Particular attention shall be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.		(3) Devices must be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to— (a) patients, taking account of the intended purpose of the device; (b) persons involved in the transport, storage and use of the device, and particular attention must be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.
10.3.Devices shall be designed and manufactured in such a way that they can be used safely with the materials and substances, including gases, with which they enter into contact during their intended use; if the devices are intended to administer medicinal products they shall be designed and manufactured in such a way as to be compatible with the medicinal products concerned in accordance with the provisions and restrictions governing those medicinal products		(4) Devices must be designed and manufactured in such a way that they can be used safely with the materials and substances, including gases, with which they enter into contact during their intended use. (5) If the devices are intended to administer medicinal products they must— (a) be designed and manufactured in such a way as to be compatible with the medicinal products concerned in accordance with the provisions and restrictions governing those medicinal products; (b) ensure that the performance of both the medicinal products and of the devices is maintained in accordance with their respective indications and intended use.

and that the performance of both the medicinal products and of the devices is maintained in accordance with their respective indications and intended use.		

10.4. Substances		Substances
10.4.1.Design and manufacture of devices Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device.		Design and manufacture of devices (6) Devices must be designed and manufactured in such a way as to reduce, as far as possible, the risks posed by substances or particles, including wear debris, degradation products and processing residues that may be released from the device.
Devices, or those parts thereof or those materials used therein that: are invasive and come into direct contact with the human body, (re)administer medicines, body liquids or other substances, including gases, to/from the body, or transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body,	This EU listing is the same as in UK (8) this section. See below UK (8) for comparison.	(7) Devices, parts of those devices or materials used in those devices listed in sub- paragraph (8) may only contain the following substances in a concentration that is above 0.1% weight where that is justified in accordance with sub-paragraph (9)—

shall only contain the following substances in a concentration that is above 0,1 % weight by weight (w/w) where justified pursuant to Section 10.4.2:		

(a) substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), of category 1A or 1B, in accordance with Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council (1), or	UK (a) gives fuller details of the EU regulation to be applied.	(a) substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), of category 1A or 1B, and on the UK mandatory classification and labelling list established and maintained in accordance with Article 38A(a) of Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006; or
(b)substances having endocrine-disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified either in accordance with the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council (2) or once a delegated act has been adopted by the Commission pursuant to the first subparagraph of Article 5(3) of Regulation (EU) No 528/2012 of the European Parliament and the Council (3), in accordance with the criteria that are relevant to human health amongst the criteria established therein.	UK (b) (i) and (ii) gives fuller details of the EU regulation to be applied	(b) substances having endocrine-disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified in accordance with— (i) the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC; or (ii) Commission Delegated Regulation (EU) 2017/2100 of 4 September 2017 setting out the scientific criteria for the determination of endocrine-disrupting properties pursuant to Regulation (EU) 528/2012 of the European Parliament and Council.

Devices, or those parts thereof or those materials used therein that: are invasive and come into direct contact with the human body, (re)administer medicines, body liquids or other substances, including gases, to/from the body, or transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body,	EU list from 10.4.1 reporduced here for comparison.	(8) The devices (or parts or materials) to which sub-paragraph (7) relates are devices which— (a) are invasive and come into direct contact with the human body; (b) administer or re-administer medicines, body liquids or other substances, including gases, to the body; or (c) transport or store medicines, body fluids or substances, including gases, to be administered or re-administered to the body.

10.4.2. Justification regarding the presence of CMR and/or endocrine-disrupting substances The justification for the presence of such substances shall be based upon: (a)an analysis and estimation of potential patient or user exposure to the substance; (b)an analysis of possible alternative substances, materials or designs, including, where available, information about independent research, peer-reviewed studies, scientific opinions from relevant scientific committees and an analysis of the availability of such alternatives; (c)argumentation as to why possible substance and/ or material substitutes, if available, or design changes, if feasible, are inappropriate in relation to maintaining the functionality, performance and the benefit-risk ratios of the product; including taking into account if the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials; and	The wording differs between these two parts but are the same requirements. See below **	(9) The justification for the presence of the substances listed in sub-paragraph (7) must be based upon— (a) an analysis and estimation of potential patient or user exposure to the substance; (b) an analysis of possible alternative substances, materials or designs, including, where available, information about independent research, peer-reviewed studies, scientific opinions from relevant scientific committees and an analysis of the availability of such alternatives; (c) arguments as to why possible substance or material substitutes, if available, or design changes, if feasible, are inappropriate in relation to maintaining the functionality, performance and the benefit-risk ratios of the product; including, where relevant having regard to the intended use of the device, taking account of the vulnerability to such substances or materials of particular patient groups including children and pregnant or breastfeeding women; (d) where applicable and available, the latest scientific guidelines relating to the risks and benefits (including the availability of alterative substances, materials, designs or treatments) of phthalates and other CMR and endocrine-disrupting substances.

(d)where applicable and available, the latest relevant scientific committee guidelines in accordance with Sections 10.4.3. and 10.4.4.		

**Part EU and UK point (d) are different but point (d) EU when taken as a whole EU 10.4.3 and 10.4.4 mean the same as point (d) UK– get the most up to date evidence on their use. This point needs to be reviewed in the future when the EU committees report and when either EU or UK legislation is updated or amended.

10.4.3.Guidelines on phthalates For the purposes of Section 10.4., the Commission shall, as soon as possible and by 26 May 2018, provide the relevant scientific committee with a mandate to prepare guidelines that shall be ready before 26 May 2020. The mandate for the committee shall encompass at least a benefit-risk assessment of the presence of phthalates which belong to either of the groups of substances referred to in points (a) and (b) of Section 10.4.1. The benefit-risk assessment shall take into account the intended purpose and context of the use of the device, as well as any available alternative substances and alternative materials, designs or medical treatments. When deemed appropriate on the basis of the latest scientific evidence, but at least every five years, the guidelines shall be updated. 10.4.4.Guidelines on other CMR and endocrine-disrupting substances Subsequently, the Commission shall mandate the relevant scientific committee to prepare guidelines as referred to in Section 10.4.3. also for other substances referred to in points (a) and (b) of Section 10.4.1., where appropriate.	This area of EU legislation is the same as UK. The UK legislation informs to use best guidance while EU legislation refers to committees see below **	

** Need to review this section when EU or UK legislation is amended or updated.

10.4.5.Labelling Where devices, parts thereof or materials used therein as referred to in Section 10.4.1. contain substances referred to in points (a) or (b) of Section 10.4.1. in a concentration above 0,1 % weight by weight (w/w), the presence of those substances shall be labelled on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging, with the list of such substances. If the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials, information on residual risks for those patient groups and, if applicable, on appropriate precautionary measures shall be given in the instructions for use.		Labelling (10) Where the devices (parts or materials) referred to in sub-paragraph (7) contain the substances in paragraph (a) and (b) of sub-paragraph (7) in a concentration above 0.1% weight by weight (w/w), the presence of those substances must— (a) be labelled on the device itself or on the packaging for each unit or, where appropriate, on the sales packaging, with the list of such substances; (b) if the intended use of such devices includes treatment of particular patient groups (including children or pregnant or breastfeeding women) who are particularly vulnerable to those substances, be contained in information on residual risks for those patient groups and, if applicable, in appropriate precautionary measures in the instructions for use.
10.5.Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress of substances into the device taking into account the device and the nature of the environment in which it is intended to be used.		(11) Devices must be designed and manufactured in such a way as to reduce, as far as possible, the risks posed by the unintentional ingress of substances into the device, taking into account the device and the nature of the environment in which it is intended to be used.

10.6.Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. Special attention shall be given to nanomaterials.		(12) Unless they come into contact with intact skin only, devices must be designed and manufactured in such a way as to reduce, as far as possible, the risks linked to the size and the properties of particles which are or can be released into the patient’s or user’s body, and special attention must be given to nanomaterials.

Essential Requirement 11. Infection and microbial contamination		Infection and microbial contamination
11.1.Devices and their manufacturing processes shall be designed in such a way as to eliminate or to reduce as far as possible the risk of infection to patients, users and, where applicable, other persons. The design shall: (a)reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries, (b) allow easy and safe handling, (c)reduce as far as possible any microbial leakage from the device and/or microbial exposure during use, and (d)prevent microbial contamination of the device or its content such as specimens or fluids.		11 .—(1) Devices and their manufacturing processes must be designed in such a way as to eliminate or to reduce as far as possible the risk of infection to patients, users and, where applicable, other persons and the design must— (a) reduce as far as possible and appropriate the risks from unintended cuts and pricks, such as needle stick injuries; (b) allow easy and safe handling; (c) reduce as far as possible any microbial leakage from the device or microbial exposure during use; (d) prevent microbial contamination of the device or its content such as specimens or fluids.
11.2.Where necessary devices shall be designed to facilitate their safe cleaning, disinfection, and/or re-sterilisation.		(2) Where necessary devices must be designed to facilitate their safe cleaning, disinfection or re-sterilisation.
11.3.Devices labelled as having a specific microbial state shall be designed, manufactured and packaged to ensure that they remain in that		(3) Devices labelled as having a specific microbial state must be designed, manufactured and packaged to ensure that they remain in that

state when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.		state when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.
11.4. Devices delivered in a sterile state shall be designed, manufactured and packaged in accordance with appropriate procedures, to ensure that they are sterile when placed on the market and that, unless the packaging which is intended to maintain their sterile condition is damaged, they remain sterile, under the transport and storage conditions specified by the manufacturer, until that packaging is opened at the point of use. It shall be ensured that the integrity of that packaging is clearly evident to the final user.		(4) Devices delivered in a sterile state must— (a) be designed, manufactured and packaged in accordance with appropriate procedures, to ensure that they are sterile when placed on the market and that, unless the packaging which is intended to maintain their sterile condition is damaged, they remain sterile, under the transport and storage conditions specified by the manufacturer, until that packaging is opened at the point of use; (b) ensure that the integrity of the packaging is clearly evident to the final user.

11.5.Devices labelled as sterile shall be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.		(5) Devices labelled as sterile must be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.
11.6.Devices intended to be sterilised shall be manufactured and packaged in appropriate and controlled conditions and facilities.		(6) Devices intended to be sterilised must be manufactured and packaged in appropriate and controlled conditions and facilities.
11.7. Packaging systems for non-sterile devices shall		(7) Packaging systems for non-sterile devices must— (a) maintain the integrity and cleanliness of the product;

maintain the integrity and cleanliness of the product and, where the devices are to be sterilised prior to use, minimise the risk of microbial contamination; the packaging system shall be suitable taking account of the method of sterilisation indicated by the manufacturer.		(b) where the devices are to be sterilised prior to use, minimise the risk of microbial contamination; (c) be suitable taking account of the method of sterilisation indicated by the manufacturer.
11.8.The labelling of the device shall distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition additional to the symbol used to indicate that devices are sterile.		(8) The labelling of the device must distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition in addition to the symbol used to indicate that devices are sterile.

Essential Requirement 12. Devices incorporating a substance considered to be a medicinal product and devices that are composed of substances or of combinations of substances that are absorbed by or locally dispersed in the human body.		Devices incorporating a substance considered to be a medicinal product and device that are composed of substances that are absorbed by or locally dispersed in the human body
12.1.In the case of devices referred to in the first subparagraph of Article 1(8), the quality, safety and usefulness of the substance which, if used separately, would be considered to be a medicinal product within the meaning of point (2) of Article 1 of Directive 2001/83/EC, shall be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC, as required by the applicable conformity assessment procedure under this Regulation.		12 - (1) In the case of devices referred to in regulation 68(8), the quality, safety and usefulness of the substance which, if used separately, would be considered to be a medicinal product within the meaning of regulation 2 of the Human Medicines Regulations 2002, must be verified by analogy with the methods specified in Annex I to Directive 2001/83/EC read subject to modifications made by the Human Medicines Regulations 2012, as required by the applicable conformity assessment procedure under Part VIII.
12.2.Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body, and that are absorbed by or locally dispersed in the human body shall comply, where applicable and in a manner limited to the aspects not covered by this Regulation, with the relevant requirements laid down in Annex I to Directive 2001/83/EC for the evaluation of absorption, distribution, metabolism, excretion, local tolerance, toxicity, interaction with other devices, medicinal products or other substances and potential		(2) Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body, and that are absorbed by or locally dispersed in the human body must comply, where applicable and in a manner limited to the aspects not covered by Part VIII, with the relevant requirements laid down in Annex I to Directive 2001/83/EC read subject to the modifications made by the Human Medicines Regulations 2012 for the evaluation of absorption, distribution, metabolism, excretion, local tolerance, toxicity, interaction with other devices, medicinal products or other substances and potential for adverse reactions, as required by the applicable conformity assessment procedure under Part VIII.

for adverse reactions, as required by the applicable conformity assessment procedure under this Regulation.		

Essential Requirement 13. Devices incorporating materials of biological origin		Devices incorporating materials of biological origin
13.1.For devices manufactured utilising derivatives of tissues or cells of human origin which are non-viable or are rendered non-viable covered by this Regulation in accordance with point (g) of Article 1(6), the following shall apply: (a)donation, procurement and testing of the tissues and cells shall be done in accordance with Directive 2004/23/EC; (b)processing, preservation and any other handling of those tissues and cells or their derivatives shall be carried out so as to provide safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents shall be addressed by appropriate methods of sourcing and by implementation of validated methods of elimination or inactivation in the course of the manufacturing process; (c)the traceability system for those devices shall be complementary and compatible with the traceability and data protection requirements laid down in Directive 2004/23/EC and in Directive 2002/98/EC.	Must be careful here as EU states EU Legislation and UK states UK legislation	13 - (1) For devices manufactured utilising derivatives of tissues or cells of human origin which are non-viable or are rendered non-viable which are covered by Part VIII in accordance with regulation 68(6)(g), the following apply— (a) donation, procurement and testing of the tissues and cells must be done in accordance with Human Tissue (Quality and Safety for Human Application) Regulations 2007; (b) processing, preservation and any other handling of those tissues and cells or their derivatives must be carried out so as to provide safety for patients, users and, where applicable, other persons and, in particular, safety with regard to viruses and other transmissible agents must be addressed by appropriate methods of sourcing and by implementation of validated methods of elimination or inactivation in the course of the manufacturing process; (c) the traceability system for those devices must be complementary and compatible with the traceability and data protection requirements laid down in Human Tissue (Quality and Safety for Human Application) Regulations 2007 and in the Blood Safety and Quality Regulations 2005.

13.2.For devices manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable the following shall apply: (a)where feasible taking into account the animal species, tissues and cells of animal origin, or their derivatives, shall originate from animals that have been subjected to veterinary controls that are adapted to the intended use of the tissues. Information on the geographical origin of the animals shall be retained by manufacturers;	Wording is slightly different but means the same.	(2) For devices manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable the following apply— (a) where feasible taking into account the animal species, tissues and cells of animal origin, or their derivatives, the tissues or cells must originate from animals that have been subjected to veterinary controls that are adapted to the intended use of the tissues and information on the geographical origin of those animals must be retained by manufacturers;

(b) sourcing, processing, preservation, testing and handling of tissues, cells and substances of animal origin, or their derivatives, shall be carried out so as to provide safety for patients, users and, where applicable, other persons. In particular safety with regard to viruses and other transmissible agents shall be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process, except when the use of such methods would lead to unacceptable degradation compromising the clinical benefit of the device;		(b) sourcing, processing, preservation, testing and handling of tissues, cells and substances of animal origin, or their derivatives, must be carried out so as to provide safety for patients, users and, where applicable, other persons; (c) safety with regard to viruses and other transmissible agents must be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process, except when the use of such methods would lead to unacceptable degradation compromising the clinical benefit of the device; (d) in the case of devices manufactured utilising tissues or cells of animal origin, or their derivatives, as referred to in the Regulation (EU) No 722/2012 the particular requirements laid down in that Regulation shall apply.

(c)in the case of devices manufactured utilising tissues or cells of animal origin, or their derivatives, as referred to in Regulation (EU) No 722/2012 the particular requirements laid down in that Regulation shall apply.		
13.3.For devices manufactured utilising non-viable biological substances other than those referred to in Sections 13.1 and 13.2, the processing, preservation, testing and handling of those substances shall be carried out so as to provide safety for patients, users and, where applicable, other persons, including in the waste disposal chain. In particular, safety with regard to viruses and other transmissible agents shall be addressed by appropriate methods of sourcing and by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.		(3) For devices manufactured utilising non-viable biological substances other than those referred to in sub-paragraphs (1) and (2), the processing, preservation, testing and handling of those substances must be carried out so as to provide safety for patients, users and, where applicable, other persons, including in the waste disposal chain and, safety with regard to viruses and other transmissible agents, must be addressed by appropriate methods of sourcing and by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.
Essential Requirement 14. Construction of devices and interaction with their environment		Construction of devices and interaction with the environment
14.1.If the device is intended for use in combination with other devices or equipment		14 .—(1) If the device is intended for use in combination with other devices or equipment— (a) the whole combination, including the connection system must be safe and must not impair the specified performance of the devices;

the whole combination, including the connection system shall be safe and shall not impair the specified performance of the devices. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use. Connections which the user has to handle, such as fluid, gas transfer, electrical or mechanical coupling, shall be designed and constructed in such a way as to minimise all possible risks, such as misconnection.		(b) any restrictions on use applying to such combinations must be indicated on the label or in the instructions for use; (c) connections which the user has to handle, such as fluid, gas transfer, electrical or mechanical coupling, must be designed and constructed in such a way as to minimise all possible risks, such as misconnection.
14.2.Devices shall be designed and manufactured in such a way as to remove or reduce as far as possible: (a)the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features; (b)risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences;		(2) Devices must be designed and manufactured in such a way as to remove or reduce as far as possible— (a) the risk of injury, in connection with their physical features, including the volume or pressure ratio, dimensional and where appropriate ergonomic features; (b) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences; (c) the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use; (d) the risks associated with the possible negative interaction between software and the information technology environment within which it operates and interacts; (e) the risks of accidental ingress of substances into the device;

(c)the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use; (d)the risks associated with the possible negative interaction between software and the IT environment within which it operates and interacts; (e) the risks of accidental ingress of substances into the device;		

(f)the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given; and (g)risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.		(f) the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given; (g) risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.
14.3.Devices shall be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition. Particular attention shall be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.		(3) Devices must be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition and particular attention must be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.
14.4.Devices shall be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively.		(4) Devices must be designed and manufactured in such a way that adjustment, calibration and maintenance can be done safely and effectively.
14.5.Devices that are intended to be operated together with other devices or products shall be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.		(5) Devices that are intended to be operate together with other devices or products must be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.

14.6.Any measurement, monitoring or display scale shall be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.		(6) Any measurement, monitoring or display scale must be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.
14.7.Devices shall be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by the user, patient or other person. To that end, manufacturers shall identify and test procedures and measures as a result of which their devices can be safely disposed after use. Such procedures shall be described in the instructions for use.	These two in essence mean the same thing safe disposal of the device and related items by users, patients, etc.	(7) In relation to the safe disposal of devices and related waste substances— (a) devices must be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by the user, patient or other person; (b) manufacturers must identify and test procedures and measures as a result of which their devices can be safely disposed after use and such procedures must be described in the instructions for use.

Essential Requirement 15. Devices with a diagnostic or measuring function		Devices with a diagnostic or measuring function
15.1.Diagnostic devices and devices with a measuring function, shall be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose, based on appropriate scientific and technical methods. The limits of accuracy shall be indicated by the manufacturer.		15 - (1) Diagnostic devices and devices with a measuring function must be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose, based on appropriate scientific and technical methods and the limits of accuracy shall be indicated by the manufacturer.
15.2.The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC (4).	Differing legislation referenced.	(2) The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Units of Measurement Regulations 1986(a).

Essential Requirement 16. Protection against radiation		Protection against radiation
16.1. General (a)Devices shall be designed, manufactured and packaged in such a way that exposure of patients, users and other persons to radiation is reduced as far as possible, and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes. (b)The operating instructions for devices emitting hazardous or potentially hazardous radiation shall contain detailed information as to the nature of the emitted radiation, the means of protecting the patient and the user, and on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate. Information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure shall also be specified.		16 – (1) Devices must be designed, manufactured and packaged in such a way that exposure of patients, users and other persons to radiation is reduced as far as possible, and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes. (2) The operating instructions for devices emitting hazardous or potentially hazardous radiation must contain— (a) detailed information as to— (i) the nature of the emitted radiation, the means of protecting the patient and the user, and; (ii) on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate; (b) information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure.

16.2. Intended radiation (a)Where devices are designed to emit hazardous, or potentially hazardous, levels of ionizing and/or non-ionizing radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent to the emission, it shall be possible for the user to control the emissions. Such devices shall be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance. (b)Where devices are intended to emit hazardous, or potentially hazardous, ionizing and/or non-ionizing radiation, they shall be fitted, where possible, with visual displays and/or audible warnings of such emissions.	The words are slightly different but the meaning is the same.	(3) Devices which are designed to emit hazardous, or potentially hazardous, levels of ionizing or non-ionizing radiation necessary for a specific medical purpose, the benefit of which is considered to outweigh the risks inherent to the emission, must— (a) make it possible for the user to control the emissions; (b) must be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance; (c) be fitted, where possible, with visual displays or audible warnings of those emissions;
16.3.Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as possible.		(d) be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as possible;

Where possible and appropriate, methods shall be selected which reduce the exposure to radiation of patients, users and other persons who may be affected.		(e) where possible and appropriate, ensure that methods are selected which reduce the exposure to radiation of patients, users and other persons who may be affected.

16.4. Ionising radiation (a)Devices intended to emit ionizing radiation shall be designed and manufactured taking into account the requirements of the Directive 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation. (b)Devices intended to emit ionising radiation shall be designed and manufactured in such a way as to ensure that, where possible, taking into account the intended use, the quantity, geometry and quality of the radiation emitted can be varied and controlled, and, if possible, monitored during treatment. (c)Devices emitting ionising radiation intended for diagnostic radiology shall be designed and manufactured in such a way as to achieve an image and/or output quality that are appropriate to the intended medical purpose whilst minimising radiation exposure of the patient and user. (d)Devices that emit ionising radiation and are intended for therapeutic radiology shall be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type, energy and, where appropriate, the quality of radiation.		(4) Devices intended to emit ionizing radiation must— (a) be designed and manufactured taking into account the requirements of any retained EU law which transposed Directive 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation; (b) be designed and manufactured in such a way as to ensure that, where possible, taking into account the intended use, the quantity, geometry and quality of the radiation emitted can be varied and controlled, and, if possible, monitored during treatment; (c) where the device is intended for diagnostic radiology, be designed and manufactured in such a way as to achieve an image or output quality that is appropriate to the intended medical purpose whilst minimising radiation exposure of the patient and user; (d) where the device is intended for therapeutic radiology, be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type, energy and, where appropriate, the quality of radiation

Essential Requirement 17. Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves		Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves
17.1.Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.		17 .—(1) Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, must— (a) be designed to ensure repeatability, reliability and performance in line with their intended use; (b) in the event of a single fault condition, be designed with appropriate means to eliminate or reduce as far as possible consequent risks or impairment of performance.
17.2.For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.		(2) For devices that incorporate software or for software that are devices in themselves, the software must be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.
17.3.Software referred to in this Section that is intended to be used in combination with mobile computing platforms shall be designed and manufactured taking into account the specific features of the mobile		(3) Software referred to in this paragraph that is intended to be used in combination with mobile computing platforms must be designed and manufactured taking into account the specific features of the mobile platform (for example size and contrast ratio of the screen)

platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).		and the external factors related to their use (varying environment as regards level of light or noise).
17.4.Manufacturers shall set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.		(4) Manufacturers must set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.
Essential Requirement 18. Active devices and devices connected to them		Active devices and devices connected to them
18.1.For non-implantable active devices, in the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks.		18 .—(1) For non-implantable active devices, in the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as possible consequent risks.
18.2.Devices where the safety of the patient depends on an internal power supply shall be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical. If necessary, such warning or indication shall be given prior to the power supply becoming critical.		(2) Devices, where the safety of the patient depends on an internal power supply, must be equipped with— (a) a means of determining the state of the power supply; (b) an appropriate warning or indication for when the capacity of the power supply becomes critical, if necessary, such warning or indication must be given prior to the power supply becoming critical.

18.3.Devices where the safety of the patient depends on an external power supply shall include an alarm system to signal any power failure.		(3) Devices where the safety of the patient depends on an external power supply must include an alarm system to signal any power failure.
18.4.Devices intended to monitor one or more clinical parameters of a patient shall be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health.		(4) Devices intended to monitor one or more clinical parameters of a patient must be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health.
18.5.Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.		(5) Devices must be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.
18.6.Devices shall be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.		(6) Devices must be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference that is adequate to enable them to operate as intended.

18.7.Devices shall be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks to the patient, user or any other person, both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.		(7) Devices must be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks to the patient, user or any other person, both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.
18.8.Devices shall be designed and manufactured in such a way as to protect, as far as possible, against unauthorised access that could hamper the device from functioning as intended.		(8) Devices must be designed and manufactured in such a way as to protect, as far as possible, against unauthorised access that could hamper the device from functioning as intended.
Essential Requirement 19. Particular requirements for active implantable devices		Particular requirements for active implantable devices
19.1. Active implantable devices shall be designed and manufactured in such a way as to remove or minimize as far as possible: (a)risks connected with the use of energy sources with particular reference, where electricity is used, to insulation, leakage currents and overheating of the devices, (b)risks connected with medical treatment, in particular those resulting from the use of defibrillators or high-frequency surgical equipment, and		19 - (1) Active implantable devices must be designed and manufactured in such a way as to remove or minimize as far as possible— (a) risks connected with the use of energy sources with particular reference, where electricity is used, to insulation, leakage currents and overheating of the devices; (b) risks connected with medical treatment, in particular those resulting from the use of defibrillators or high- frequency surgical equipment; (c) risks which may arise where maintenance and calibration are impossible, including— (i) excessive increase of leakage currents; (ii) ageing of the materials used;

(c)risks which may arise where maintenance and calibration are impossible, including: — excessive increase of leakage currents, — ageing of the materials used, — excess heat generated by the device, — decreased accuracy of any measuring or control mechanism.		(iii) excess heat generated by the device; (iv) decreased accuracy of any measuring or control mechanism.
19.2. Active implantable devices shall be designed and manufactured in such a way as to ensure —if applicable, the compatibility of the devices with the substances they are intended to administer, and — the reliability of the source of energy.		(2) Active implantable devices must be designed and manufactured in such a way as to ensure— (a) if applicable, the compatibility of the devices with the substances they are intended to administer; (b) the reliability of the source of energy.
19.3.Active implantable devices and, if appropriate, their component parts shall be identifiable to allow any necessary measure to be taken following the discovery of a potential risk in connection with the devices or their component parts.		(3) Active implantable devices and, if appropriate, their component parts must be identifiable to allow any necessary measure to be taken following the discovery of a potential risk in connection with the devices or their component parts.

19.4. Active implantable devices shall bear a code by which they and their manufacturer can be unequivocally identified (particularly with regard to the type of device and its year of manufacture); it shall be possible to read this code, if necessary, without the need for a surgical operation.		(4) Active implantable devices must bear a code— (a) by which they and their manufacturer can be unequivocally identified (particularly with regard to the type of device and its year of manufacture); and (b) which it is possible to read, if necessary, without the need for a surgical operation.
Essential Requirement 20. Protection against mechanical and thermal risks		Protection against mechanical and thermal risks
20.1.Devices shall be designed and manufactured in such a way as to protect patients and users against mechanical risks connected with, for example, resistance to movement, instability and moving parts.		20 .—(1) Devices must be designed and manufactured in such a way as to protect patients and users against mechanical risks connected with, for example, resistance to movement, instability and moving parts.
20.2.Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.		(2) Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.

20.3.Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.		(3) Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.
20.4.Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, shall be designed and constructed in such a way as to minimise all possible risks.		(4) Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, must be designed and constructed in such a way as to minimise all possible risks.
20.5. Errors likely to be made when fitting or refitting certain parts which could be a source of risk shall be made impossible by the design and construction of such parts or, failing this, by information given on the parts themselves and/or their housings. The same information shall be given on moving parts and/or their housings where the direction of movement needs to be known in order to avoid a risk.		(5) Errors likely to be made when fitting or refitting certain parts which could be a source of risk — (a) must be made impossible by the design and construction of such parts or by information given on the parts themselves or their housings; and (b) must contain the same information on moving parts or their housings where the direction of movement needs to be known in order to avoid a risk.

20.6.Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings shall not attain potentially dangerous temperatures under normal conditions of use.		(6) Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal conditions of use.

Essential Requirement 21. Protection against the risks posed to the patient or user by devices supplying energy or substances		Protection against the risks posed to the patient or user by devices supplying energy or substances
21.1.Devices for supplying the patient with energy or substances shall be designed and constructed in such a way that the amount to be delivered can be set and maintained accurately enough to ensure the safety of the patient and of the user.		21 .—(1) Devices for supplying the patient with energy or substances must be designed and constructed in such a way that the amount to be delivered can be set and maintained accurately enough to ensure the safety of the patient and of the user.
21.2. Devices shall be fitted with the means of preventing and/or indicating any inadequacies in the amount of energy delivered or substances delivered which could pose a danger. Devices shall incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy or substances from an energy and/or substance source.		(2) Devices must— (a) be fitted with the means of preventing or indicating any inadequacies in the amount of energy delivered or substances delivered which could pose a danger; (b) incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy or substances from an energy and/or substance source.
21.3. The function of the controls and indicators shall be clearly specified on the devices.		(3) The function of the controls and indicators— (a) must be clearly specified on devices; (b) where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual

Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information shall be understandable to the user and, as appropriate, the patient.		system, such information must be understandable to the user and, as appropriate, the patient.
Essential Requirement 22. Protection against the risks posed by medical devices intended by the manufacturer for use by lay persons		Protection against the risks posed by medical devices intended by the manufacturer for use by lay persons
22.1. Devices for use by lay persons shall be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to lay persons and the influence resulting from variation that can be reasonably anticipated in the lay person's technique and environment. The information and instructions provided by the manufacturer shall be easy for the lay person to understand and apply.		22 .—(1) Devices for use by lay persons must— (a) be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to lay persons and the influence resulting from variation that can be reasonably anticipated in the lay person's technique and environment; and (b) be provided by the manufacturer with information and instructions which are easy for the lay person to understand and apply.
22.2. Devices for use by lay persons shall be designed and manufactured in such a way as to:		(2) Devices for use by lay persons must be designed and manufactured in such a way as to— (a) ensure that the device can be used safely and accurately by the intended user at all stages of the procedure, if necessary after appropriate training or information;

—ensure that the device can be used safely and accurately by the intended user at all stages of the procedure, if necessary after appropriate training and/or information, —reduce, as far as possible and appropriate, the risk from unintended cuts and pricks such as needle stick injuries, and —reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, in the interpretation of the results.		(b) reduce, as far as possible and appropriate, the risk from unintended cuts and pricks such as needle stick injuries; and (c) reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, in the interpretation of the results.
22.3. Devices for use by lay persons shall, where appropriate, include a procedure by which the lay person: —can verify that, at the time of use, the device will perform as intended by the manufacturer, and —if applicable, is warned if the device has failed to provide a valid result.		(3) Devices for use by lay persons must, where appropriate, include a procedure by which the lay person— (a) can verify that, at the time of use, the device will perform as intended by the manufacturer; (b) is warned if the device has failed to provide a valid result.

CHAPTER III RDING THE INFORMATION SUPPLIED WITH THE DEVICE		PART 3 Requirements regarding instructions for use

Essential Requirement 23. Label and instructions for use		Label and instructions for use
23.1.General requirements regarding the information supplied by the manufacturer Each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user, or any other person, as appropriate. Such information may appear on the device itself, on the packaging or in the instructions for use, and shall, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following:		23 .—(1) Each device must be accompanied by the information (which may appear on the device itself, on the packaging or in the instructions for use) needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user, or any other person, as appropriate.
(a)The medium, format, content, legibility, and location of the label and instructions for use shall be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use shall be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams. (b)The information required on the label shall be provided on the device itself. If this is not practicable or appropriate, some or all of the		(a) that the medium, format, content, legibility, and location of the label and instructions for use must be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended users and, in particular, instructions for use must be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams; (b) the information required on the label must be provided on the device itself or, if this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit, or on the packaging of multiple devices;

information may appear on the packaging for each unit, and/or on the packaging of multiple devices.		

(c)Labels shall be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification ('RFID') or bar codes. (d)Instructions for use shall be provided together with devices. By way of exception, instructions for use shall not be required for class I and class IIa devices if such devices can be used safely without any such instructions and unless otherwise provided for elsewhere in this Section. (e)Where multiple devices are supplied to a single user and/or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge. (f)Instructions for use may be provided to the user in non-paper format (e.g. electronic) to the extent, and only under the conditions, set out in Regulation (EU) No 207/2012 or in any subsequent implementing rules adopted pursuant to this Regulation.	Watch out for point F as this may vary in future EU and UK legislation This bit has a variation –	(c) labels must be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification ('RFID') or bar codes; (d) in general, instructions for use must be provided together with devices but, by way of exception, instructions for use are not required for Class I and Class IIa devices if such devices can be used safely without any such instructions and unless otherwise provided for elsewhere in this paragraph; (e) where multiple devices are supplied to a single user or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge; (f) instructions for use may be provided to the user in non-paper format (for example electronic) to the extent, and only under the conditions, set out in Regulation (EU) No 207/2012; (g) residual risks which are required to be communicated to the user or other person must be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer; (h) where appropriate, the information supplied by the manufacturer —

(g)Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer. (h) Where appropriate, the information supplied by the manufacturer shall take the form of internationally recognised symbols. Any symbol or identification colour used shall conform to the harmonised standards or CS. In areas for which no harmonised standards or CS exist, the symbols and colours shall be described in the documentation supplied with the device.	CS. In EU legislation this is Common specifications.	(i) must take the form of internationally recognised symbols; (ii) must conform, in terms of any symbol or identification colour used, to the relevant standards; and (iii) in areas for which no relevant standards exist, the symbols and colours must be described in the documentation supplied with the device.

23.2. Information on the label The label shall bear all of the following particulars: (a) the name or trade name of the device; (b)the details strictly necessary for a user to identify the device, the contents of the packaging and, where it is not obvious for the user, the intended purpose of the device; (c)the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business; (d)if the manufacturer has its registered place of business outside the Union, the name of the authorised representative and address of the registered place of business of the authorised representative; (e)where applicable, an indication that the device contains or incorporates: —a medicinal substance, including a human blood or plasma derivative, or — tissues or cells, or their derivatives, of human origin, or		Information on the label (4) The label must bear the following particulars— (a) the name or trade name of the device; (b) the details strictly necessary for a user to identify the device, the contents of the packaging and, where it is not obvious for the user, the intended purpose of the device; (c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business; (d) if the manufacturer has its registered place of business outside the United Kingdom, the name and address of the person placing the device on the market; (e) where applicable, an indication that the device contains or incorporates— (i) a medicinal substance, including a human blood or plasma derivative, or tissues or cells, or their derivatives, of human origin; or (ii) tissues or cells of animal origin, or their derivatives, as referred to in Regulation (EU) No 722/2012; (f) where applicable, information labelled in accordance with paragraph 10(10); (g) the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate;

—tissues or cells of animal origin, or their derivatives, as referred to in Regulation (EU) No 722/2012; (f)where applicable, information labelled in accordance with Section 10.4.5.; (g)the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate; (h)the UDI carrier referred to in Article 27(4) and Part C of Annex VII;		(h) the UDI carrier referred to in regulation 91(4) and Part C of Schedule 8;
(i)an unambiguous indication of t the time limit for using or implanting the device safely, expressed at least in terms of year and month, where this is relevant; (j)where there is no indication of the date until when it may be used safely, the date of manufacture. This date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable; (k)an indication of any special storage and/or handling condition that applies;		(i) an unambiguous indication of the time limit for using or implanting the device safely, expressed at least in terms of year and month, where this is relevant; (j) where there is no indication of the date until when it may be used safely, the date of manufacture and this date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable; (k) an indication of any special storage or handling condition that applies; (l) if the device is supplied sterile, an indication of its sterile state and the sterilisation method; (m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device, and to any other person (this information may be kept to a minimum in which case,

(l)if the device is supplied sterile, an indication of its sterile state and the sterilisation method; (m)warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device, and to any other person. This information may be kept to a minimum in which case more detailed information shall appear in the instructions for use, taking into account the intended users; (n)if the device is intended for single use, an indication of that fact. A manufacturer's indication of single use shall be consistent across the Union; (o)if the device is a single-use device that has been reprocessed, an indication of that fact, the number of reprocessing cycles already performed, and any limitation as regards the number of reprocessing cycles; (p) if the device is custom-made, the words 'custom-made device';		more detailed information must appear in the instructions for use, taking into account the intended users); (n) if the device is intended for single use, an indication of that fact; (o) if the device is a single-use device that has been reprocessed, an indication of that fact, the number of reprocessing cycles already performed, and any limitation as regards the number of reprocessing cycles; (p) if the device is custom-made, the words 'custom-made device';

(q)an indication that the device is a medical device. If the device is intended for clinical investigation only, the words 'exclusively for clinical investigation'; (r)in the case of devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body, the overall qualitative composition of the device and quantitative information on the main constituent or constituents responsible for achieving the principal intended action; (s)for active implantable devices, the serial number, and for other implantable devices, the serial number or the lot number.		(q) an indication that the device is a medical device and, if the device is intended for clinical investigation only, the words 'exclusively for clinical investigation'; (r) in the case of devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body, the overall qualitative composition of the device and quantitative information on the main constituent or constituents responsible for achieving the principal intended action; (s) for active implantable devices, the serial number, and for other implantable devices, the serial number or the lot number.
23.3. Information on the packaging which maintains the sterile condition of a device ('sterile packaging') The following particulars shall appear on the sterile packaging: (a)an indication permitting the sterile packaging to be recognised as such,		(5) Where packaging maintains the sterile condition of the device ("sterile packaging") t he following particulars must appear on that sterile packaging— (a) an indication permitting the sterile packaging to be recognised as such; (b) a declaration that the device is in a sterile condition; (c) the method of sterilisation;

(b) a declaration that the device is in a sterile condition, (c) the method of sterilisation, (d) the name and address of the manufacturer, (e) a description of the device, (f)if the device is intended for clinical investigations, the words 'exclusively for clinical investigations', (g) if the device is custom-made, the words 'custom-made device',		(d) the name and address of the manufacturer; (e) a description of the device; (f) if the device is intended for clinical investigations, the words 'exclusively for clinical investigations'; (g) if the device is custom-made, the words 'custom-made device'; .

(h) the month and year of manufacture, (i)an unambiguous indication of the time limit for using or implanting the device safely expressed at least in terms of year and month, and (j)an instruction to check the instructions for use for what to do if the sterile packaging is damaged or unintentionally opened before use.		(h) the month and year of manufacture; (i) an unambiguous indication of the time limit for using or implanting the device safely expressed at least in terms of year and month; (j) an instruction to check the instructions for use for what to do if the sterile packaging is damaged or unintentionally opened before use

23.4. Information in the instructions for use The instructions for use shall contain all of the following particulars: (a)the particulars referred to in points (a), (c), (e), (f), (k), (l), (n) and (r) of Section 23.2; (b)the device's intended purpose with a clear specification of indications, contra-indications, the patient target group or groups, and of the intended users, as appropriate; (c)where applicable, a specification of the clinical benefits to be expected. (d)where applicable, links to the summary of safety and clinical performance referred to in Article 32; (e) the performance characteristics of the device; (f)where applicable, information allowing the healthcare professional to verify if the device is suitable and select the corresponding software and accessories;		Information in instructions for use (6) The instructions for use must contain all the following particulars— (a) the particulars referred to in paragraphs (a), (c), (e), (f), (k), (l), (n) and (r) of paragraph 23(4); (b) the device's intended purpose with a clear specification of indications, contra- indications, the patient target group or groups, and of the intended users, as appropriate; (c) where applicable, a specification of the clinical benefits to be expected; (d) where applicable, links to the summary of safety and clinical performance referred to in regulation 96; (e) the performance characteristics of the device; (f) where applicable, information allowing the healthcare professional to verify if the device is suitable and select the corresponding software and accessories; (g) any residual risks, contra-indications and any undesirable side-effects, including information to be conveyed to the patient in this regard; (h) specifications the user requires to use the device appropriately, for example if the device has a measuring function, the degree of accuracy claimed for it; (i) details of any preparatory treatment or handling of the device before it is ready for use or during its use, such as sterilisation, final assembly, calibration, including the levels of disinfection required

(g)any residual risks, contra-indications and any undesirable side-effects, including information to be conveyed to the patient in this regard; (h)specifications the user requires to use the device appropriately, e.g. if the device has a measuring function, the degree of accuracy claimed for it; (i)details of any preparatory treatment or handling of the device before it is ready for use or during its use, such as sterilisation, final assembly, calibration, etc., including the levels of disinfection required to ensure patient safety and all available methods for achieving those levels of disinfection;		to ensure patient safety and all available methods for achieving those levels of disinfection;

(j)any requirements for special facilities, or special training, or particular qualifications of the device user and/or other persons; (k)the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant: —details of the nature, and frequency, of preventive and regular maintenance, and of any preparatory cleaning or disinfection, —identification of any consumable components and how to replace them, —information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime, and —methods for eliminating the risks encountered by persons involved in installing, calibrating or servicing devices; (l)if the device is supplied sterile, instructions in the event of the sterile packaging being damaged or unintentionally opened before use; (m)if the device is supplied non-sterile with the intention that it is sterilised before use, the appropriate instructions for sterilisation;		(j) any requirements for special facilities, or special training, or particular qualifications of the device user or other persons; (k) the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant— (i) details of the nature, and frequency, of preventive and regular maintenance, and of any preparatory cleaning or disinfection; (ii) identification of any consumable components and how to replace them; (iii) information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime; (iv) methods for eliminating the risks encountered by persons involved in installing, calibrating or servicing devices; (l) if the device is supplied sterile, instructions in the event of the sterile packaging being damaged or unintentionally opened before use; (m) if the device is supplied non-sterile with the intention that it is sterilised before use, the appropriate instructions for sterilisation; (n) if the device is reusable, information must be provided— (i) on the appropriate processes for allowing reuse, including cleaning, disinfection, packaging and, where appropriate, the validated method of re- sterilisation; and (ii) to identify when the device should no longer be reused, for example signs of material degradation or the maximum number of allowable reuses;

(n) if the device is reusable, information on the appropriate processes for allowing reuse, including cleaning, disinfection, packaging and, where appropriate, the validated method of re-sterilisation appropriate to the Member State or Member States in which the device has been placed on the market. Information shall be provided to identify when the device should no longer be reused, e.g. signs of material degradation or the maximum number of allowable reuses;		

(o)an indication, if appropriate, that a device can be reused only if it is reconditioned under the responsibility of the manufacturer to comply with the general safety and performance requirements; (p)if the device bears an indication that it is for single use, information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used. This information shall be based on a specific section of the manufacturer's risk management documentation, where such characteristics and technical factors shall be addressed in detail. If in accordance with point (d) of Section 23.1. no instructions for use are required, this information shall be made available to the user upon request; (q)for devices intended for use together with other devices and/or general purpose equipment: —information to identify such devices or equipment, in order to obtain a safe combination, and/or		(o) an indication, if appropriate, that a device can be reused only if it is reconditioned under the responsibility of the manufacturer to comply with the general safety and performance requirements; (p) if the device bears an indication that it is for single use— (i) information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used; (ii) the information must be based on a specific section of the manufacturer’s risk management documentation, where such characteristics and technical factors must be addressed in detail; (iii) if, in accordance with sub-paragraph (3)(d), no instructions for use are required, this information must be made available to the user upon request; (q) for devices intended for use together with other devices or general purpose equipment— (i) information to identify such devices or equipment, in order to obtain a safe combination; (ii) information on any known restrictions to combinations of devices and equipment;

—information on any known restrictions to combinations of devices and equipment;		

(r) if the device emits radiation for medical purposes: —detailed information as to the nature, type and where appropriate, the intensity and distribution of the emitted radiation, —the means of protecting the patient, user, or other person from unintended radiation during use of the device; (s)information that allows the user and/or patient to be informed of any warnings, precautions, contra-indications, measures to be taken and limitations of use regarding the device. That information shall, where relevant, allow the user to brief the patient about any warnings, precautions, contra-indications, measures to be taken and limitations of use regarding the device. The information shall cover, where appropriate: —warnings, precautions and/or measures to be taken in the event of malfunction of the device or changes in its performance that may affect safety, —warnings, precautions and/or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical		(r) if the device emits radiation for medical purposes— (i) detailed information as to the nature, type and where appropriate, the intensity and distribution of the emitted radiation; (ii) the means of protecting the patient, user, or other person from unintended radiation during use of the device; (s) information that allows the user or patient to be informed of, or as the case may be, briefed about any warnings, precautions, contra-indications, measures to be taken and limitations of use regarding the device and this information must cover, where appropriate— (i) warnings, precautions or measures to be taken in the event of malfunction of the device or changes in its performance that may affect safety; (ii) warnings, precautions or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature; (iii) warnings, precautions or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, or therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment;

and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature, —warnings, precautions and/or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, or therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment, —if the device is intended to administer medicinal products, tissues or cells of human or animal origin, or their derivatives, or biological substances, any limitations or incompatibility in the choice of substances to be delivered, —warnings, precautions and/or limitations related to the medicinal substance or biological material that is incorporated into the device as an integral part of the device; and —precautions related to materials incorporated into the device that contain or consist of CMR substances or endocrine-disrupting substances, or that could result in sensitisation or an allergic reaction by the patient or user;		(iv) if the device is intended to administer medicinal products, tissues or cells of human or animal origin, or their derivatives, or biological substances, any limitations or incompatibility in the choice of substances to be delivered; (v) warnings, precautions or limitations related to the medicinal substance or biological material that is incorporated into the device as an integral part of the device; and (vi) precautions related to materials incorporated into the device that contain or consist of CMR substances or endocrine-disrupting substances, or that could result in sensitisation or an allergic reaction by the patient or user;

(t)in the case of devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body, warnings and precautions, where appropriate, related to the general profile of interaction of the device and its products of metabolism with other devices, medicinal products and other substances as well as contra-indications, undesirable side-effects and risks relating to overdose; (u)in the case of implantable devices, the overall qualitative and quantitative information on the materials and substances to which patients can be exposed; (v)warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories and the consumables used with it, if any. This information shall cover, where appropriate:		(t) in the case of devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body, warnings and precautions, where appropriate, related to— (i) the general profile of interaction of the device and its products of metabolism with other devices, medicinal products and other substances; (ii) contra-indications, undesirable side-effects and risks relating to overdose; (u) in the case of implantable devices, the overall qualitative and quantitative information on the materials and substances to which patients can be exposed; (v) warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories and the consumables used with it, which must, where appropriate cover— (i) infection or microbial hazards such as explants, needles or surgical equipment contaminated with potentially infectious substances of human origin, and (ii) physical hazards such as from sharps; (iii) if, in accordance with the sub-paragraph (3)(d), no instructions for use are required, this information must be made available to the user upon request;

—infection or microbial hazards such as explants, needles or surgical equipment contaminated with potentially infectious substances of human origin, and — physical hazards such as from sharps. If in accordance with the point (d) of Section 23.1 no instructions for use are required, this information shall be made available to the user upon request; (w)for devices intended for use by lay persons, the circumstances in which the user should consult a healthcare professional; (x)for the devices covered by this Regulation pursuant to Article 1(2), information regarding the absence of a clinical benefit and the risks related to use of the device;		(w)for devices intended for use by lay persons, the circumstances in which the user should consult a healthcare professional; (x) for the devices covered by Part VIII of these Regulations pursuant to regulation 68(2)(b), information regarding the absence of a clinical benefit and the risks related to use of the device;
(y)date of issue of the instructions for use or, if they have been revised, date of issue and identifier of the latest revision of the instructions for use; (z)a notice to the user and/or patient that any serious incident that has occurred in relation to the device should be reported to the		(y)the date of issue of the instructions for use or, if they have been revised, the date of issue and the identifier of the latest revision of the instructions for use; (z) a notice to the user or patient that any serious incident that has occurred in relation to the device should be reported to the manufacturer and to the Secretary of State;

manufacturer and the competent authority of the Member State in which the user and/or patient is established; (aa)information to be supplied to the patient with an implanted device in accordance with Article 18; (ab)for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.		(aa) information to be supplied to the patient with an implanted device in accordance with regulation 83; (bb) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, Information Technology networks characteristics and Information Technology security measures, including protection against unauthorised access, necessary to run the software as intended.

(1) Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

(2) Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (OJ L 396, 30.12.2006, p. 1).

(3) Regulation (EU) No 528/2012 of the European Parliament and the Council of 22 May 2012 concerning the making available on the market of and use of biocidal products (OJ L 167, 27.6.2012, p. 1).

(4) Council Directive 80/181/EEC of 20 December 1979 on the approximation of the laws of the Member States relating to units of measurement and on the repeal of Directive 71/354/EEC (OJ L 39, 15.2.1980, p. 40).

Appendix C4 4 Comparison: In Vitro Diagnostic Devices EU with UK General Safety and Performance Requirements.

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU		2019 No. 791 EXITING THE EUROPEAN UNION CONSUMER PROTECTION The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 Made - 1st April 2019
ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS CHAPTER I GENERAL REQUIREMENTS		SCHEDULE 17 Regulation 1A General safety and performance requirements- in vitro diagnostic medical devices PART 1 General requirements for in vitro diagnostic medical devices
1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.		1. Devices must— (a) achieve the performance intended by their manufacturer; (b) be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose; (c) be safe and effective; (d) not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.
2. The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.		2. The requirement in this Schedule to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.

3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall: (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability; and (f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.		3.—(1) Manufacturers must establish, implement, document and maintain a risk management system. (2) Risk management must be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating and in carrying out risk management manufacturers must— (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in sub-paragraph (c) in accordance with the requirements of paragraph 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability; (f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of paragraph 4.

4. Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, the manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority: (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users. Manufacturers shall inform users of any residual risks.		4.—(1) Risk control measures adopted by manufacturers for the design and manufacture of the devices must conform to safety principles, taking account of the generally acknowledged state of the art. (2) To reduce risks, the manufacturers must manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. (3) In selecting the most appropriate solutions, manufacturers must, in the following order of priority— (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; (c) provide information for safety (warnings, precautions, contra-indications) and, where appropriate, training to users; (d) inform users of any residual risks.
5. In eliminating or reducing risks related to use error, the manufacturer shall: (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).		5. In eliminating or reducing risks related to use error, the manufacturer must— (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety); (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).

6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.		6. The characteristics and performance of a device must not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer’s instructions.
7. Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.		7. Devices must be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.
8. All known and foreseeable risks, and any undesirable effects shall be minimised and be acceptable when weighed against the evaluated potential benefits to the patients and/or the user arising from the intended performance of the device during normal conditions of use.		8. All known and foreseeable risks, and any undesirable effects must be minimised and be acceptable when weighed against the evaluated potential benefits to the patients or the user arising from the intended performance of the device during normal conditions of use.

CHAPTER II REQUIREMENTS REGARDING PERFORMANCE, DESIGN AND MANUFACTURE		PART 2 Requirements regarding design and manufacture of in vitro diagnostic medical devices
Essential Requirement 9 Performance characteristics		Performance characteristics
9.1. Devices shall be designed and manufactured in such a way that they are suitable for the purposes referred to in point (2) of Article 2, as specified by the manufacturer, and suitable with regard to the performance they are intended to achieve, taking account of the generally acknowledged state of the art. They shall achieve the performances, as stated by the manufacturer and in particular, where applicable: (a) the analytical performance, such as, analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off, including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference, cross-reactions; and (b) the clinical performance, such as diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations.		9.—(1) Devices must— (a) be designed and manufactured in such a way that they are suitable for one or more of the purposes listed in the definition of "in vitro diagnostic medical device" in regulation 137, as specified by the manufacturer, and suitable with regard to the performance they are intended to achieve, taking account of the generally acknowledged state of the art; b) achieve the performances, as stated by the manufacturer and in particular, where applicable— (i) the analytical performance, such as, analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off, including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference, cross- reactions; (ii) the clinical performance, such as diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations
9.2. The performance characteristics of the device shall be maintained during the lifetime of the device as indicated by the manufacturer.		2) The performance characteristics of the device must be maintained during the lifetime of the device as indicated by the manufacturer.

9.3. Where the performance of devices depends on the use of calibrators and/or control materials, the metrological traceability of values assigned to calibrators and/or control materials shall be assured through suitable reference measurement procedures and/or suitable reference materials of a higher metrological order. Where available, metrological traceability of values assigned to calibrators and control materials shall be assured to certified reference materials or reference measurement procedures.		(3) Where the performance of devices depends on the use of calibrators or control materials— (a) the metrological traceability of values assigned to calibrators or control materials must be assured through suitable reference measurement procedures or suitable reference materials of a higher metrological order; (b) where available, metrological traceability of values assigned to calibrators and control materials must be assured to certified reference materials or reference measurement procedures.
9.4. The characteristics and performances of the device shall be specifically checked in the event that they may be affected when the device is used for the intended use under normal conditions: (a) for devices for self-testing, performances obtained by laypersons; (b) for devices for near-patient testing, performances obtained in relevant environments (for example, patient home, emergency units, ambulances).		(4) The characteristics and performances of the device must be specifically checked in the event that they may be affected when the device is used for the intended use under normal conditions— (a) for devices for self-testing, performances obtained by laypersons; (b) for devices for near-patient testing, performances obtained in relevant environments (for example, patient home, emergency units, ambulances).

Essential Requirement 10 Chemical, physical and biological properties	A NA	Chemical physical and biological properties
10.1. Devices shall be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Chapter I are fulfilled. Particular attention shall be paid to the possibility of impairment of analytical performance due to physical and/or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected (such as biological tissues, cells, body fluids and micro-organisms), taking account of the intended purpose of the device.		10 (1) Devices must be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Part 1 are fulfilled and, in this regard, particular attention must be paid to the possibility of impairment of analytical performance due to physical or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected (such as biological tissues, cells, body fluids and micro-organisms), taking account of the intended purpose of the device.
10.2. Devices shall be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to patients, taking account of the intended purpose of the device, and to the persons involved in the transport, storage and use of the devices. Particular attention shall be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.10.3. Devices shall be designed and manufactured in such a way as to reduce to a level as low as reasonably practicable the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), in accordance with Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council (1), and to substances having endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health	Not the same words but the same meaning.	(2) As regards substances or particles that may be released from the device— (a) devices must be designed and manufactured in such a way as to reduce to a level as low as reasonably practicable the risks posed by these substances or particles, including wear debris, degradation products and processing residues; (b) special attention must be given to substances— (i) which are carcinogenic, mutagenic or toxic to reproduction ('CMR') and on the UK mandatory classification and labelling list established and maintained in accordance with Article 38A of Regulation (EC) No 1272/2008 of the European Parliament and of the Council; and (ii) with endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified in accordance with the procedure set out in Article

and which are identified in accordance with the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council (2).		59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council.

10.4. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress of substances into the device, taking into account the device and the nature of the environment in which it is intended to be used.		(3) Devices must be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress of substances into the device, taking into account the device and the nature of the environment in which it is intended to be used.

11.1. Devices and their manufacturing processes shall be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the user or, where applicable, other persons. The design shall: (a) allow easy and safe handling; (b) reduce as far as possible any microbial leakage from the device and/or microbial exposure during use; and, where necessary (c) prevent microbial contamination of the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen.		11 - (1) Devices and their manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the user or, where applicable, other persons and the design must— (a) allow easy and safe handling; (b) reduce, as far as possible, any microbial leakage from the device or microbial exposure during use; (c) where necessary, prevent microbial contamination of the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen.
11.2. Devices labelled either as sterile or as having a specific microbial state shall be designed, manufactured and packaged to ensure that their sterile condition or microbial state is maintained under the transport and storage conditions specified by the manufacturer until that packaging is opened at the point of use, unless the packaging which maintains their sterile condition or microbial state is damaged.		(2) Devices labelled either as sterile or as having a specific microbial state must be designed, manufactured and packaged to ensure that their sterile condition or microbial state is maintained under the transport and storage conditions specified by the manufacturer until that packaging is opened at the point of use, unless the packaging which maintains their sterile condition or microbial state is damaged.
11.3. Devices labelled as sterile shall be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.		(3) Devices labelled as sterile must be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.
11.4. Devices intended to be sterilised shall be manufactured and packaged in appropriate and controlled conditions and facilities.		(4) Devices intended to be sterilised must be manufactured and packaged in appropriate and controlled conditions and facilities.

11.5. Packaging systems for non-sterile devices shall maintain the integrity and cleanliness of the product and, where the devices are to be sterilised prior to use, minimise the risk of microbial contamination; the packaging system shall be suitable taking account of the method of sterilisation indicated by the manufacturer.		(5) Packaging systems for non-sterile devices must— (a) maintain the integrity and cleanliness of the product and, where the devices are to be sterilised prior to use, minimise the risk of microbial contamination; (b) be suitable taking account of the method of sterilisation indicated by the manufacturer.
11.6. The labelling of the device shall distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition additional to the symbol used to indicate that devices are sterile.		(6) The labelling of the device must distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition additional to the symbol used to indicate that devices are sterile.

Essential Requirement 12 Devices incorporating materials of biological origin		Devices incorporating materials of a biological origin
Where devices include tissues, cells and substances of animal, human or microbial origin, the selection of sources, the processing, preservation, testing and handling of tissues, cells and substances of such origin and control procedures shall be carried out so as to provide safety for user or other person. In particular, safety with regard to microbial and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This might not apply to certain devices if the activity of the microbial and other transmissible agent are integral to the intended purpose of the device or when such elimination or inactivation process would compromise the performance of the device.		12. Where devices include tissues, cells and substances of animal, human or microbial origin— (a) the selection of sources, the processing, preservation, testing and handling of tissues, cells and substances of such origin and control procedures must be carried out so as to provide safety for users or other persons; (b) safety with regard to microbial and other transmissible agents must be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process but this requirement would not apply to devices if the activity of the microbial and other transmissible agent are integral to the intended purpose of the device or when such elimination or inactivation process would compromise the performance of the device.

Essential Requirement 13. Construction of devices and interaction with their environment		Construction of devices and interaction with the environment
13.1. If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system, shall be safe and shall not impair the specified performances of the devices. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use.		13 - (1) If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system, must be safe and must not impair the specified performances of the devices and any restrictions on use applying to such combinations must be indicated on the label and in the instructions for use.
13.2. Devices shall be designed and manufactured in such a way as to remove or reduce as far as possible: (a) the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features; (b) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences; (c) the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use; (d) the risks associated with the possible negative interaction between software and the IT environment within which it operates and interacts; (e) the risks of accidental ingress of substances into the device; (f) the risk of incorrect identification of specimens and the risk of erroneous results due to, for example, confusing colour and/or numeric and/or character codings on specimen receptacles,		(2) Devices must be designed and manufactured in such a way as to remove or reduce as far as possible— (a) the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features; (b) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences; (c) the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use; (d) the risks associated with the possible negative interaction between software and the IT environment within which it operates and interacts; (e) the risks of accidental ingress of substances into the device; (f) the risk of incorrect identification of specimens and the risk of erroneous results due to, for example, confusing colour or numeric or character codings on specimen receptacles,

removable parts and/or accessories used with devices in order to perform the test or assay as intended; (g) the risks of any foreseeable interference with other devices.		removable parts or accessories used with devices in order to perform the test or assay as intended; (g) the risks of any foreseeable interference with other devices.

13.3. Devices shall be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition. Particular attention shall be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.		(3) Devices must be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition and, in this regard, particular attention must be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.
13.4. Devices shall be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively.		(4) Devices must be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively.
13.5. Devices that are intended to be operated together with other devices or products shall be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.		(5) Devices that are intended to be operated together with other devices or products must be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.
13.6. Devices shall be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by users, or other person. To that end, manufacturers shall identify and test procedures and measures as a result of which their devices can be safely disposed after use. Such procedures shall be described in the instructions for use.		(6) Devices must be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by users, or other persons and, in doing so manufacturers must— (a) identify and test procedures and measures as a result of which their devices can be safely disposed after use;

		(b) ensure that such test procedures are described in the instructions for use.
13.7 The measuring, monitoring or display scale (including colour change and other visual indicators) shall be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.		(7) The measuring, monitoring or display scale (including colour change and other visual indicators) must be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.

Essential Requirement 14. Devices with a measuring function	A NA	Devices with a measuring function
14.1. Devices having a primary analytical measuring function shall be designed and manufactured in such a way as to provide appropriate analytical performance in accordance with point (a) of Section 9.1 of Annex I, taking into account the intended purpose of the device.		14 .—(1) Devices having a primary analytical measuring function must be designed and manufactured in such a way as to provide appropriate analytical performance in accordance with paragraph 9(1), taking into account the intended purpose of the device.
14.2. The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC (3).		(2) The measurements made by devices with a measuring function must be expressed in legal units conforming to the provisions of the Units of Measurement Regulations 1986.

Essential Requirement 15. Protection against radiation		Protection against radiation
15.1. Devices shall be designed, manufactured and packaged in such a way that exposure of users or other persons to radiation (intended, unintended, stray or scattered) is reduced as far as possible and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for diagnostic purposes.		15 - (1) Devices must be designed, manufactured and packaged in such a way that exposure of users or other persons to radiation (intended, unintended, stray or scattered) is reduced as far as possible and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for diagnostic purposes.
15.2. When devices are intended to emit hazardous, or potentially hazardous, ionizing and/or non-ionizing radiation, they shall as far as possible be: (a) designed and manufactured in such a way as to ensure that the characteristics and the quantity of radiation emitted can be controlled and/or adjusted; and (b) fitted with visual displays and/or audible warnings of such emissions.		(2) When devices are intended to emit hazardous, or potentially hazardous, ionizing or non-ionizing radiation, they must as far as possible be— (a) designed and manufactured in such a way as to ensure that the characteristics and the quantity of radiation emitted can be controlled or adjusted; (b) fitted with visual displays or audible warnings of such emissions.
15.3. The operating instructions for devices emitting hazardous or potentially hazardous radiation shall contain detailed information as to the nature of the emitted radiation, the means of protecting the user, and on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate. Information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure shall also be specified.		(3) The operating instructions for devices emitting hazardous or potentially hazardous radiation must contain— (a) detailed information as to the nature of the emitted radiation, the means of protecting the user, and on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate; (b) information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure.

Essential Requirement 16. Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves.		Electronic programmable systems- devices that incorporate programmable systems and software that are devices in themselves
16.1. Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.		16 - (1) Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, must— (a) be designed to ensure repeatability, reliability and performance in line with their intended use; (b) in the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.
16.2. For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.		(2) For devices that incorporate software or for software that is a device in itself , the software must be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.
16.3. Software referred to in this Section that is intended to be used in combination with mobile computing platforms shall be designed and manufactured taking into account the specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).		(3) Software referred to in this paragraph that is intended to be used in combination with mobile computing platforms must be designed and manufactured taking into account the specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).
16.4. Manufacturers shall set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.		(4) Manufacturers must set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.

Essential Requirement. 17. Devices connected to or equipped with an energy source		Devices connected to or equipped with an energy source
17.1. For devices connected to or equipped with an energy source, in the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks.		17 - (1) For devices connected to or equipped with an energy source, in the event of a single fault condition, appropriate means must be adopted to eliminate or reduce as far as possible consequent risks.
17.2. Devices where the safety of the patient depends on an internal power supply shall be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical. If necessary, such warning or indication shall be given prior to the power supply becoming critical.		(2) Devices where the safety of the patient depends on an internal power supply must be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical and if necessary, such warning or indication shall be given prior to the power supply becoming critical.
17.3. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.		(3) Devices must be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.
17.4. Devices shall be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.		(4) Devices must be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.
17.5. Devices shall be designed and manufactured in such a way as to avoid as far as possible the risk of accidental electric shocks to the user, or other person both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.		(5) Devices must be designed and manufactured in such a way as to avoid as far as possible the risk of accidental electric shocks to the user, or other person both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.

Essential Requirement. 18. Protection against mechanical and thermal risks		Protection against mechanical and thermal risks
18.1. Devices shall be designed and manufactured in such a way as to protect users and other persons against mechanical risks.		18 .—(1) Devices must be designed and manufactured in such a way as to protect users and other persons against mechanical risks.
18.2. Devices shall be sufficiently stable under the foreseen operating conditions. They shall be suitable to withstand stresses inherent to the foreseen working environment, and to retain this resistance during the expected lifetime of the devices, subject to any inspection and maintenance requirements as indicated by the manufacturer.		(2) Devices must— (a) be sufficiently stable under the foreseen operating conditions; (b) be suitable to withstand stresses inherent to the foreseen working environment, and to retain this resistance during the expected lifetime of the devices, subject to any inspection and maintenance requirements as indicated by the manufacturer.
18.3. Where there are risks due to the presence of moving parts, risks due to break-up or detachment, or leakage of substances, then appropriate protection means shall be incorporated. Any guards or other means included with the device to provide protection, in particular against moving parts, shall be secure and shall not interfere with access for the normal operation of the device, or restrict routine maintenance of the device as intended by the manufacturer.		(3) Where there are risks due to the presence of moving parts, risks due to break-up or detachment, or leakage of substances, then appropriate protection means must be incorporated. (4) Any guards or other means included with the device to provide protection, in particular against moving parts, must be secure and must not interfere with access for the normal operation of the device, or restrict routine maintenance of the device as intended by the manufacturer.
18.4. Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.		(5) Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.

18.5. Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.		(6) Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.
18.6. Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, shall be designed and constructed in such a way as to minimise all possible risks.		(7) Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, must be designed and constructed in such a way as to minimise all possible risks.
18.7. Errors likely to be made when fitting or refitting certain parts which could be a source of risk shall be made impossible by the design and construction of such parts or, failing this, by information given on the parts themselves and/or their housings. The same information shall be given on moving parts and/or their housings where the direction of movement needs to be known in order to avoid a risk.		(8) Errors likely to be made when fitting or refitting certain parts which could be a source of risk must be made impossible by the design and construction of such parts or, failing this, by information given on the parts themselves or their housings. (9) Information must be given on moving parts or their housings where the direction of movement needs to be known in order to avoid a risk.
18.8. Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings shall not attain potentially dangerous temperatures under normal conditions of use.		(10) Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal conditions of use.

Essential Requirement. 19. Protection against the risks posed by devices intended for self-testing or near-patient testing		Protection against the risks posed by devices intended for self-testing or near-patient testing
19.1. Devices intended for self-testing or near-patient testing shall be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to the intended user and the influence resulting from variation that can be reasonably anticipated in the intended user's technique and environment. The information and instructions provided by the manufacturer shall be easy for the intended user to understand and apply in order to correctly interpret the result provided by the device and to avoid misleading information. In the case of near-patient testing, the information and the instructions provided by the manufacturer shall make clear the level of training, qualifications and/or experience required by the user.		19 .—(1) Devices intended for self-testing or near-patient testing— (a) must be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to the intended user and the influence resulting from variation that can be reasonably anticipated in the intended user's technique and environment; (b) the information and instructions provided by the manufacturer must be easy for the intended user to understand and apply in order to correctly interpret the result provided by the device and to avoid misleading information; (c) in the case of near-patient testing, the information and the instructions provided by the manufacturer must make clear the level of training, qualifications or experience required by the user.
19.2. Devices intended for self-testing or near-patient testing shall be designed and manufactured in such a way as to: (a) ensure that the device can be used safely and accurately by the intended user at all stages of the procedure if necessary after appropriate training and/or information; and (b) reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, the specimen, and also in the interpretation of the results.		(2) Devices intended for self-testing or near-patient testing must be designed and manufactured in such a way as to— (a) ensure that the device can be used safely and accurately by the intended user at all stages of the procedure if necessary after appropriate training or information; (b) reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, the specimen, and also in the interpretation of the results.

19.3. Devices intended for self-testing and near-patient testing shall, where feasible, include a procedure by which the intended user: (a) can verify that, at the time of use, the device will perform as intended by the manufacturer; and (b) be warned if the device has failed to provide a valid result.		(3) Devices intended for self-testing and near-patient testing must, where feasible, include a procedure by which the intended user— (a) can verify that, at the time of use, the device will perform as intended by the manufacturer; (b) be warned if the device has failed to provide a valid result.

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CHAPTER III REQUIREMENTS REGARDING INFORMATION SUPPLIED WITH THE DEVICE		PART 3 Requirements regarding information supplied with the device
Essential Requirement. 20. Label and instructions for use		Labels and instructions for use
20.1. General requirements regarding the information supplied by the manufacturer Each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user or any other person, as appropriate. Such information may appear on the device itself, on the packaging or in the instructions for use, and shall, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following: (a) The medium, format, content, legibility, and location of the label and instructions for use shall be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use shall be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams. (b) The information required on the label shall be provided on the device itself. If this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit. If individual full labelling of each unit is not practicable, the information shall be set out on the packaging of multiple devices.		General requirements regarding the information supplied by the manufacturer 20 - (1) Each device must be accompanied— (a) by the information needed to identify the device and its manufacturer; (b) by any safety and performance information relevant to the user or any other person, as appropriate. (2) The information in paragraph (1) may appear on the device itself, on the packaging or in the instructions for use, and must, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following— (a) the medium, format, content, legibility, and location of the label and instructions for use must be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user and, in particular, instructions for use must be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams; (b) the information required on the label must be provided on the device itself or if this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit and, if

		individual full labelling of each unit is not practicable, the information must be set out on the packaging of multiple devices;

(c) Labels shall be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification or bar codes. (d) Instructions for use shall be provided together with devices. However, in duly justified and exceptional cases instructions for use shall not be required or may be abbreviated if the device can be used safely and as intended by the manufacturer without any such instructions for use. (e) Where multiple devices, with the exception of devices intended for self-testing or near-patient testing, are supplied to a single user and/or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge. (f) When the device is intended for professional use only, instructions for use may be provided to the user in non-paper format (e.g. electronic), except when the device is intended for near-patient testing. (g) Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer.		(c) labels must be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification or bar codes; (d) instructions for use must be provided together with devices but, in duly justified and exceptional cases, instructions for use are not required, or may be abbreviated, if the device can be used safely and as intended by the manufacturer without any such instructions for use; (e) where multiple devices, with the exception of devices intended for self-testing or near-patient testing, are supplied to a single user or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge; (f) when the device is intended for professional use only, instructions for use may be provided to the user in non-paper format (e.g. electronic), except when the device is intended for near-patient testing; (g) residual risks which are required to be communicated to the user or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer;

(h) Where appropriate, the information supplied by the manufacturer shall take the form of internationally recognised symbols, taking into account the intended users. Any symbol or identification colour used shall conform to the harmonised standards or CS. In areas for which no harmonised standards or CS exist, the symbols and colours shall be described in the documentation supplied with the device.		(h) where appropriate, the information supplied by the manufacturer— (i) must take the form of internationally recognised symbols, taking into account the intended users; (ii) must conform, in terms of any symbols or identification colour used, to the designated standards or CS; (iii) in areas for which no designated standards or CS exist, the symbols and colours must be described in the documentation supplied with the device;
(i) In the case of devices containing a substance or a mixture which may be considered as being dangerous, taking account of the nature and quantity of its constituents and the form under which they are present, (ii) relevant hazard pictograms and labelling requirements of Regulation (EC) No 1272/2008 shall apply. (iii) Where there is insufficient space to put all the information on the device itself or on its label, the relevant hazard pictograms shall be put on the label and the other information required by Regulation (EC) No 1272/2008 shall be given in the instructions for use. (j) The provisions of Regulation (EC) No 1907/2006 on the safety data sheet shall apply, unless all relevant information, as appropriate, is already made available in the instructions for use.		(i) in the case of devices containing a substance or a mixture which may be considered as being dangerous, taking account of the nature and quantity of its constituents and the form under which they are present— (i) relevant hazard pictograms and labelling requirements of Regulation (EC) No 1272/2008 apply; or (ii) where there is insufficient space to put all the information on the device itself or on its label, the relevant hazard pictograms must be put on the label and the other information required by Regulation (EC) No 1272/2008 must be given in the instructions for use; (j) the provisions of Regulation (EC) No 1907/2006 on the safety data sheet must apply, unless all relevant information, as appropriate, is already made available in the instructions for use.
20.2. Information on the label The label shall bear all of the following particulars:		Information on the label (3) The label must bear all of the following particulars—

(a) the name or trade name of the device; (b) the details strictly necessary for a user to identify the device and, where it is not obvious for the user, the intended purpose of the device; (c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business; (d) if the manufacturer has its registered place of business outside the Union, the name of its authorised representative and the address of the registered place of business of the authorised representative; (e) an indication that the device is an in vitro diagnostic medical device, or if the device is a 'device for performance study', an indication of that fact; (f) the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate; (g) the UDI carrier as referred to in Article 24 and Part C of Annex VI; (h) an unambiguous indication of the time limit for using the device safely, without degradation of performance, expressed at least in terms of year and month and, where relevant, the day, in that order; (i) where there is no indication of the date until when it may be used safely, the date of manufacture. This date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable;		(a) the name or trade name of the device; (b) the details strictly necessary for a user to identify the device and, where it is not obvious for the user, the intended purpose of the device; (c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business; (d) if the manufacturer has its registered place of business outside the United Kingdom, the name and address of the person placing the device on the market; (e) an indication that the device is an in vitro diagnostic medical device, or if the device is a 'device for performance study', an indication of that fact; (f) the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate; (g) the UDI carrier as referred to in regulation 157 and Part C of Schedule 22; (h) an unambiguous indication of the time limit for using the device safely, without degradation of performance, expressed at least in terms of year and month and, where relevant, the day, in that order; (i) where there is no indication of the date until when it may be used safely, the date of manufacture and this date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable;

(j) where relevant, an indication of the net quantity of contents, expressed in terms of weight or volume, numerical count, or any combination of thereof, or other terms which accurately reflect the contents of the package; (k) an indication of any special storage and/or handling condition that applies; (l) where appropriate, an indication of the sterile state of the device and the sterilisation method, or a statement indicating any special microbial state or state of cleanliness; (m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device or to any other person. This information may be kept to a minimum in which case more detailed information shall appear in the instructions for use, taking into account the intended users; (n) if the instructions for use are not provided in paper form in accordance with point (f) of Section 20.1, a reference to their accessibility (or availability), and where applicable the website address where they can be consulted; (o) where applicable, any particular operating instructions; (p) if the device is intended for single use, an indication of that fact. A manufacturer's indication of single use shall be consistent across the Union; (q) if the device is intended for self-testing or near-patient testing, an indication of that fact; (r) where rapid assays are not intended for self-testing or near-patient testing, the explicit exclusion hereof;	Note how the UK legislation does not look outside of UK – see point (p)	(j) where relevant, an indication of the net quantity of contents, expressed in terms of weight or volume, numerical count, or any combination of thereof, or other terms which accurately reflect the contents of the package; (k) an indication of any special storage or handling condition that applies; (l) where appropriate, an indication of the sterile state of the device and the sterilisation method, or a statement indicating any special microbial state or state of cleanliness; (m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device or to any other person (this information may be kept to a minimum in which case more detailed information must appear in the instructions for use, taking into account the intended users); (n) if the instructions for use are not provided in paper form in accordance with paragraph 20(2)(f), a reference to their accessibility (or availability), and where applicable the website address where they can be consulted; (o) where applicable, any particular operating instructions; (p) if the device is intended for single use, an indication of that fact; (q) if the device is intended for self-testing or near-patient testing, an indication of that fact; (r) where rapid assays are not intended for self-testing or near-patient testing, the explicit exclusion thereof;

(s) where device kits include individual reagents and articles that are made available as separate devices, each of those devices shall comply with the labelling requirements contained in this Section and with the requirements of this Regulation; (t) the devices and separate components shall be identified, where applicable in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components. As far as practicable and appropriate, the information shall be set out on the device itself and/or, where appropriate, on the sales packaging; (u) the label for devices for self-testing shall bear the following particulars: (i) the type of specimen(s) required to perform the test (e.g. blood, urine or saliva); (ii) the need for additional materials for the test to function properly; (iii) contact details for further advice and assistance. The name of devices for self-testing shall not reflect an intended purpose other than that specified by the manufacturer.		(4) The following additional labelling requirements apply to these specific devices— (a) for device kits which include individual reagents and articles that are made available as separate devices, the labelling requirements contained in sub- paragraph (3) and requirements of Part IX apply to each device; (b) devices and separate components must be identified, where applicable in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components and, as far as practicable and appropriate, the information must be set out on the device itself and, where appropriate, on the sales packaging; (c) the label for devices for self-testing must bear the following particulars— (i) the type of specimens required to perform the test (for example blood, urine or saliva); (ii) the need for additional materials for the test to function properly; (iii) contact details for further advice and assistance; (d) the name of devices for self-testing must not reflect an intended purpose other than that specified by the manufacturer.

20.3. Information on the packaging which maintains the sterile condition of a device ('sterile packaging'): The following particulars shall appear on the sterile packaging: (a) an indication permitting the sterile packaging to be recognised as such, (b) a declaration that the device is in a sterile condition, (c) the method of sterilisation, (d) the name and address of the manufacturer, (e) a description of the device, (f) the month and year of manufacture, (g) an unambiguous indication of the time limit for using the device safely, expressed at least in terms of year and month and, where relevant, the day, in that order, (h) an instruction to check the instructions for use for what to do if the sterile packaging is damaged or unintentionally opened before use.		Information on the packaging which maintains the sterile condition of a device ('sterile packaging') (5) The following particulars must appear on the sterile packaging— (a) an indication permitting the sterile packaging to be recognised as such; (b) a declaration that the device is in a sterile condition; (c) the method of sterilisation; (d) the name and address of the manufacturer; (e) description of the device; (f) the month and year of manufacture; (g) an unambiguous indication of the time limit for using the device safely, expressed at least in terms of year and month and, where relevant, the day, in that order.
20.4. Information in the instructions for use 20.4.1. The instructions for use shall contain all of the following particulars: (a) the name or trade name of the device; (b) the details strictly necessary for the user to uniquely identify the device; (c) the device's intended purpose: (i) what is detected and/or measured;		Information in the instructions for use (6) The instructions for use must contain all of the following particulars— (a) the name or trade name of the device; (b) the details strictly necessary for the user to uniquely identify the device; (c) the device's intended purpose in terms of— (i) what is detected or measured;

(ii) its function (e.g. screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic); (iii) the specific information that is intended to be provided in the context of: — a physiological or pathological state; — congenital physical or mental impairments; — the predisposition to a medical condition or a disease; — the determination of the safety and compatibility with potential recipients; — the prediction of treatment response or reactions; — the definition or monitoring of therapeutic measures; (iv) whether it is automated or not; (v) whether it is qualitative, semi-quantitative or quantitative; (vi) the type of specimen(s) required; (vii) where applicable, the testing population; and (viii) for companion diagnostics, the International Non-proprietary Name (INN) of the associated medicinal product for which it is a companion test. (d) an indication that the device is an in vitro diagnostic medical device, or, if the device is a 'device for performance study', an indication of that fact;		(ii) its function (for example screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic); (iii) the specific information that is intended to be provided in the context of— (aa) a physiological or pathological state; (bb) congenital physical or mental impairments; (cc) the predisposition to a medical condition or a disease; (dd) the determination of the safety and compatibility with potential recipients; (ee) the prediction of treatment response or reactions; (ff) the definition or monitoring of therapeutic measures; (iv) whether it is automated or not; (v) whether it is qualitative, semi-quantitative or quantitative; (vi) the type of specimens required; (vii) where applicable, the testing population; (viii) for companion diagnostics, the International Non-proprietary Name (INN) of the associated medicinal product for which it is a companion test; (d) an indication that the device is an in vitro diagnostic medical device, or, if the device is a 'device for performance study', an indication of that fact;
(e) the intended user, as appropriate (e.g. self-testing, near patient and laboratory professional use, healthcare professionals); (f) the test principle; (g) a description of the calibrators and controls and any limitation upon their use (e.g. suitable for a dedicated instrument only); (h) a description of the reagents and any limitation upon their use (e.g. suitable for a dedicated instrument only) and the composition		(e) the intended user, as appropriate (for example self-testing, near patient and laboratory professional use, healthcare professionals); (f) the test principle; (g) a description of the calibrators and controls and any limitation upon their use (for example suitable for a dedicated instrument only);

of the reagent product by nature and amount or concentration of the active ingredient(s) of the reagent(s) or kit as well as a statement, where appropriate, that the device contains other ingredients which might influence the measurement; (i) a list of materials provided and a list of special materials required but not provided; (j) for devices intended for use in combination with or installed with or connected to other devices and/or general purpose equipment: — information to identify such devices or equipment, in order to obtain a validated and safe combination, including key performance characteristics, and/or — information on any known restrictions to combinations of devices and equipment. (k) an indication of any special storage (e.g. temperature, light, humidity, etc.) and/or handling conditions which apply; (l) in-use stability which may include the storage conditions, and shelf life following the first opening of the primary container, together with the storage conditions and stability of working solutions, where this is relevant;		(h) a description of the reagents and any limitation upon their use (for example suitable for a dedicated instrument only) and the composition of the reagent product by nature and amount or concentration of the active ingredient of the reagent or kit as well as a statement, where appropriate, that the device contains other ingredients which might influence the measurement; (i) a list of materials provided and a list of special materials required but not provided; (j) for devices intended for use in combination with or installed with or connected to other devices or general purpose equipment— (i) information to identify such devices or equipment, in order to obtain a validated and safe combination, including key performance characteristics; (ii) information on any known restrictions to combinations of devices and equipment; (k) an indication of any special storage (for example temperature, light, humidity, etc.) or handling conditions which apply; (l) in-use stability which may include the storage conditions, and shelf life following the first opening of the primary container, together with the storage conditions and stability of working solutions, where this is relevant;

(m) if the device is supplied as sterile, an indication of its sterile state, the sterilisation method and instructions in the event of the sterile packaging being damaged before use; (n) information that allows the user to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the device. That information shall cover, where appropriate: (i) warnings, precautions and/or measures to be taken in the event of malfunction of the device or its degradation as suggested by changes in its appearance that may affect performance, (ii) warnings, precautions and/or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature, (iii) warnings, precautions and/or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment, (iv) precautions related to materials incorporated into the device that contain or consist of CMR substances, or endocrine disrupting substances or that could result in sensitisation or an allergic reaction by the patient or user,		(m) if the device is supplied as sterile, an indication of its sterile state, the sterilisation method and instructions in the event of the sterile packaging being damaged before use; (n) information that allows the user to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the device, that information must, where appropriate, cover— (i) warnings, precautions or measures to be taken in the event of malfunction of the device or its degradation as suggested by changes in its appearance that may affect performance; (ii) warnings, precautions or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature, (iii) warnings, precautions or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment; (iv) precautions related to materials incorporated into the device that contain or consist of CMR substances, or endocrine disrupting substances or that could result in sensitisation or an allergic reaction by the patient or user; (v) if the device is intended for single use, an indication of that fact;

(v) if the device is intended for single use, an indication of that fact. A manufacturer's indication of single use shall be consistent across the Union,		

(vi) if the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, decontamination, packaging and, where appropriate, the validated method of re-sterilisation. Information shall be provided to identify when the device should no longer be reused, such as signs of material degradation or the maximum number of allowable reuses; (o) any warnings and/or precautions related to potentially infectious material that is included in the device; (p) where relevant, requirements for special facilities, such as a clean room environment, or special training, such as on radiation safety, or particular qualifications of the intended user; (q) conditions for collection, handling, and preparation of the specimen; (r) details of any preparatory treatment or handling of the device before it is ready for use, such as sterilisation, final assembly, calibration, etc., for the device to be used as intended by the manufacturer; (s) the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant:		(vi) if the device is reusable— (aa) information on the appropriate processes to allow reuse, including cleaning, disinfection, decontamination, packaging and, where appropriate, the validated method of re-sterilisation, (bb) information on when the device should no longer be used such as signs of material degradation or the maximum number of allowable reuses; (o) any warnings or precautions related to potentially infectious material that is included in the device; (p) where relevant, requirements for special facilities, such as a clean room environment, or special training, such as on radiation safety, or particular qualifications of the intended user; (q) conditions for collection, handling, and preparation of the specimen; (r) details of any preparatory treatment or handling of the device before it is ready for use, such as sterilisation, final assembly, calibration, etc., for the device to be used as intended by the manufacturer; (s) the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant—

— details of the nature, and frequency, of preventive and regular maintenance, including cleaning and disinfection; — identification of any consumable components and how to replace them; — information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime; — methods for mitigating the risks encountered by persons involved in installing, calibrating or servicing devices. (t) where applicable, recommendations for quality control procedures;		(i) details of the nature, and frequency, of preventive and regular maintenance, including cleaning and disinfection; (ii) identification of any consumable components and how to replace them; (iii) information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime; (iv) methods for mitigating the risks encountered by persons involved in installing, calibrating or servicing devices; (t) where applicable, recommendations for quality control procedures;
(u) the metrological traceability of values assigned to calibrators and control materials, including identification of applied reference materials and/or reference measurement procedures of higher order and information regarding maximum (self-allowed) batch to batch variation provided with relevant figures and units of measure; (v) assay procedure including calculations and interpretation of results and where relevant if any confirmatory testing shall be considered; where applicable, the instructions for use shall be accompanied by information regarding batch to batch variation provided with relevant figures and units of measure; (w) analytical performance characteristics, such as analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and measurement range, (information needed for the control of known relevant		(u) the metrological traceability of values assigned to calibrators and control materials, including identification of applied reference materials or reference measurement procedures of higher order and information regarding maximum (self-allowed) batch to batch variation provided with relevant figures and units of measure; (v) assay procedure including calculations and interpretation of results and where relevant if any confirmatory testing is to be considered; (w) where applicable, the instructions for use shall be accompanied by information regarding batch to batch variation provided with relevant figures and units of measure; (x) analytical performance characteristics, such as analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and measurement

interferences, cross-reactions and limitations of the method), measuring range, linearity and information about the use of available reference measurement procedures and materials by the user; (x) clinical performance characteristics as defined in Section 9.1 of this Annex; (y) the mathematical approach upon which the calculation of the analytical result is made;		range, (information needed for the control of known relevant interferences, cross- reactions and limitations of the method), measuring range, linearity and information about the use of available reference measurement procedures and materials by the user; (y) clinical performance characteristics as defined in paragraph 9(1) of this Schedule; (z) the mathematical approach upon which the calculation of the analytical result is made;
(z) where relevant, clinical performance characteristics, such as threshold value, diagnostic sensitivity and diagnostic specificity, positive and negative predictive value; (aa) where relevant, reference intervals in normal and affected populations; (ab) information on interfering substances or limitations (e.g. visual evidence of hyperlipidaemia or haemolysis, age of specimen) that may affect the performance of the device; (ac) warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories, and the consumables used with it, if any. This information shall cover, where appropriate: (i) infection or microbial hazards, such as consumables contaminated with potentially infectious substances of human origin; (ii) environmental hazards such as batteries or materials that emit potentially hazardous levels of radiation); (iii) physical hazards such as explosion.		(aa) where relevant, clinical performance characteristics, such as threshold value, diagnostic sensitivity and diagnostic specificity, positive and negative predictive value; (bb) where relevant, reference intervals in normal and affected populations; (cc) information on interfering substances or limitations (for example visual evidence of hyperlipidaemia or haemolysis, age of specimen) that may affect the performance of the device; (dd) warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories, and the consumables used with it, if any which, where appropriate, must cover— (i) infection or microbial hazards, such as consumables contaminated with potentially infectious substances of human origin; (ii) environmental hazards such as batteries or materials that emit potentially hazardous levels of radiation);

(ad) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business at which he can be contacted and its location be established, together with a telephone number and/or fax number and/or website address to obtain technical assistance; (ae) date of issue of the instructions for use or, if they have been revised, date of issue and identifier of the latest revision of the instructions for use, with a clear indication of the introduced modifications; (af) a notice to the user that any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established;		(iii) physical hazards such as explosion; (ee) the name, registered trade name or registered trade mark of the manufacturer and the address of their registered place of business at which they can be contacted and their location be established, together with a telephone number or fax number or website address to obtain technical assistance; (ff) date of issue of the instructions for use or, if they have been revised, date of issue and identifier of the latest revision of the instructions for use, with a clear indication of the introduced modifications; (gg) a notice to the user that any serious incident that has occurred in relation to the device must be reported to the manufacturer and to the Secretary of State;
(ag) where device kits include individual reagents and articles that may be made available as separate devices, each of these devices shall comply with the instructions for use requirements contained in this Section and with the requirements of this Regulation; (ah) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.	EU legislation paragraphs 20.4.1 (ag) and (ah) are noted in UK legislation point 20 – 7 (a) and 20 – 7 (b)	(7) The following additional requirements relating to the instructions for use apply to these specific devices— (a) for device kits which include individual reagents and articles that may be made available as separate devices, each of these devices must comply with the instructions for use requirements contained in this sub-paragraph (6) and with the requirements of Part IX; (b) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.

20.4.2 In addition, the instructions for use for devices intended for self-testing shall comply with all of the following principles: (a) details of the test procedure shall be given, including any reagent preparation, specimen collection and/or preparation and information on how to run the test and interpret the results; (b) specific particulars may be omitted provided that the other information supplied by the manufacturer is sufficient to enable the user to use the device and to understand the result(s) produced by the device; (c) the device's intended purpose shall provide sufficient information to enable the user to understand the medical context and to allow the intended user to make a correct interpretation of the results; (d) the results shall be expressed and presented in a way that is readily understood by the intended user; (e) information	UK legislation point 20 – 7 (a) and 20 – 7 (b) are noted in EU legislation paragraphs 20.4.1 (ag) and (ah)	(7) The following additional requirements relating to the instructions for use apply to these specific devices— (a) for device kits which include individual reagents and articles that may be made available as separate devices, each of these devices must comply with the instructions for use requirements contained in this sub-paragraph (6) and with the requirements of Part IX; (b) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended. (c) the instructions for use for devices intended for self-testing must comply with all of the following principles— (i) details of the test procedure shall be given, including any reagent preparation, specimen collection or preparation and information on how to run the test and interpret the results; (ii) specific particulars may be omitted provided that the other information supplied by the manufacturer is sufficient to enable the user to use the device and to understand the results produced by the device; (iii) the device’s intended purpose must provide sufficient information to enable the user to understand the medical context and to allow the intended user to make a correct interpretation of the results; (iv) the results must be expressed and presented in a way that is readily understood by the intended user;

shall be provided with advice to the user on action to be taken (in case of positive, negative or indeterminate result), on the test limitations and on the possibility of false positive or false negative result. Information shall also be provided as to any factors that can affect the test result such as age, gender, menstruation, infection, exercise, fasting, diet or medication; (f) the information provided shall include a statement clearly directing that the user should not take any decision of medical relevance without first consulting the appropriate healthcare professional, information on disease effects and prevalence, and, where available, information specific to the Member State(s) where the device is placed on the market on where a user can obtain further advice such as national helplines, websites; (g) for devices intended for self-testing used for the monitoring of a previously diagnosed existing disease or condition, the information shall specify that the patient should only adapt the treatment if he has received the appropriate training to do so.		(v) information— (aa) must be provided with advice to the user on action to be taken (in case of positive, negative or indeterminate result), on the test limitations and on the possibility of false positive or false negative result; (bb) must also be provided as to any factors that can affect the test result such as age, gender, menstruation, infection, exercise, fasting, diet or medication; (vi) the information provided must include a statement clearly directing that the user should not take any decision of medical relevance without first consulting the appropriate healthcare professional, information on disease effects and prevalence, and, where available, information on where a user can obtain further advice such as helplines, websites; (d) for devices intended for self-testing used for the monitoring of a previously diagnosed existing disease or condition, the information must specify that the patient should only adapt the treatment if he has received the appropriate training to do so.

(1) Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

(2) Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (OJ L 136, 29.5.2007, p. 3).

(3) Council Directive 80/181/EEC of 20 December 1979 on the approximation of the laws of the Member States relating to units of measurement and on the repeal of Directive 71/354/EEC (OJ L 39, 15.2.1980, p. 40).

Appendix C4 5 Comparison: Technical Documentation Requirements EU with UK

In Vitro Diagnostic Devices.

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU		2019 No. 791 EXITING THE EUROPEAN UNION CONSUMER PROTECTION The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 Made - 1st April 2019
Annex II		SCHEDULE 18 Regulation 1A
TECHNICAL DOCUMENTATION The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular the elements listed in this Annex.		Technical documentation- in vitro diagnostic medical devices 1. The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer must be presented in a clear, organised, readily searchable and unambiguous manner and must include in particular the elements listed in this Schedule.
1.Device description and specification, including variants and accessories		Device description and specification, including variants and accessories
1.1. Device description and specification (a) product or trade name and a general description of the device including its intended purpose and intended users;	As appropriate pointing to the appropriate part of either EU or UK legislation.	Device description and specification 2.—(1) The description and specification of the device must contain the following— (a) product or trade name and a general description of the device including its intended purpose and intended users;

(b) the Basic UDI-DI as referred to in Part C of Annex VI assigned by the manufacturer to the device in question, as soon as identification of this device becomes based on a UDI system, or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability;		(b) the Basic UDI-DI as referred to in Part C of Schedule 22 assigned by the manufacturer to the device in question, as soon as identification of this device becomes based on a UDI system, or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability;

(c) the intended purpose of the device which may include information on: (i) what is to be detected and/or measured; (ii) its function such as screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic; (iii) the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate; (iv) whether it is automated or not; (v) whether it is qualitative, semi-quantitative or quantitative; (vi) the type of specimen(s) required; (vii) where applicable, the testing population; (viii) the intended user; (ix) in addition, for companion diagnostics, the relevant target population and the associated medicinal product(s). (d) the description of the principle of the assay method or the principles of operation of the instrument; (e) the rationale for the qualification of the product as a device; (f) the risk class of the device and the justification for the classification rule(s) applied in accordance with Annex VIII;	As appropriate pointing to the appropriate part of either EU or UK legislation.	(c) the intended purpose of the device which may include information on— (i) what is to be detected or measured; (ii) its function such as screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic; (iii) the specific disorder, condition or risk factor of interest that it is intended to detect, define or differentiate; (iv) whether it is automated or not; (v) whether it is qualitative, semi-quantitative or quantitative; (vi) the type of specimen required; (vii) where applicable, the testing population; (viii) the intended user; (ix) in addition, for companion diagnostics, the relevant target population and the associated medicinal products; (d) the description of the principle of the assay method or the principles of operation of the instrument; (e) the rationale for the qualification of the product as a device; (f) the risk class of the device and the justification for the classification rules applied in accordance with Schedule 23;

(g) the description of the components and where appropriate, the description of the reactive ingredients of relevant components such as antibodies, antigens, nucleic acid primers; and where applicable: (h) the description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use; (i) for instruments of automated assays: the description of the appropriate assay characteristics or dedicated assays; (j) for automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation; (k) a description of any software to be used with the device; (l) a description or complete list of the various configurations/variants of the device that are intended to be made available on the market; (m) a description of the accessories for a device, other devices and other products that are not devices, which are intended to be used in combination with the device.		(g) the description of the components and where appropriate, the description of the reactive ingredients of relevant components such as antibodies, antigens, nucleic acid primers; (h) where applicable, the description of the specimen collection and transport materials provided with the device or descriptions of specifications recommended for use; (i) where applicable, for instruments of automated assays, the description of the appropriate assay characteristics or dedicated assays; (j) where applicable, for automated assays, a description of the appropriate instrumentation characteristics or dedicated instrumentation; k) where applicable, a description of any software to be used with the device; (l) where applicable, a description or complete list of the various configurations or variants of the device that are intended to be made available on the market; (m) where applicable, a description of the accessories for a device, other devices and other products that are not devices, which are intended to be used in combination with the device.

1.2. Reference to previous and similar generations of the device (a) an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist; (b) an overview of identified similar devices available on the Union or international markets, where such devices exist.		Reference to previous and similar generations of the device (2) Where applicable the technical documentation must contain— (a) an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist; (b) an overview of identified similar devices available on international markets, where such devices exist.

2. INFORMATION TO BE SUPPLIED BY THE MANUFACTURER		Information to be supplied by the manufacturer
A complete set of (a) the label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in the case of specific management conditions, in the languages accepted in the Member States where the device is envisaged to be sold; (b) the instructions for use in the languages accepted in the Member States where the device is envisaged to be sold.	Note UK legislation only requires English.	3. The manufacturer must supply a complete set of— (a) the label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in the case of specific management conditions, in English; (b) the instructions for use in English.

3. DESIGN AND MANUFACTURING INFORMATION		Design and manufacturing information
3.1. Design information Information to allow the design stages applied to the device to be understood shall include: (a) a description of the critical ingredients of the device such as antibodies, antigens, enzymes and nucleic acid primers provided or recommended for use with the device; (b) for instruments, a description of major subsystems, analytical technology such as operating principles and control mechanisms, dedicated computer hardware and software; (c) for instruments and software, an overview of the entire system; (d) for software, a description of the data interpretation methodology, namely the algorithm; (e) for devices intended for self-testing or near-patient testing, a description of the design aspects that make them suitable for self-testing or near-patient testing.		Design information 4. - (1) Information to allow the design stages applied to the device to be understood must include— (a) a description of the critical ingredients of the device such as antibodies, antigens, enzymes and nucleic acid primers provided or recommended for use with the device; (b) for instruments, a description of major subsystems, analytical technology such as operating principles and control mechanisms, dedicated computer hardware and software; (c) for instruments and software, an overview of the entire system; (d) for software, a description of the data interpretation methodology, namely the algorithm; (e) for devices intended for self-testing or near-patient testing, a description of the design aspects that make them suitable for self-testing or near-patient testing.
3.2. Manufacturing information (a) information to allow the manufacturing processes such as production, assembly, final product testing, and packaging of the finished device to be understood. More detailed information shall be provided for the audit of the quality management system or other applicable conformity assessment procedures; (b) identification of all sites, including suppliers and sub-contractors, where manufacturing activities are performed.		Manufacturing information (2) Manufacturing information must include— (a) information to allow the manufacturing processes such as production, assembly, final product testing, and packaging of the finished device to be understood (more detailed information must be provided for the audit of the quality management system or other applicable conformity assessment procedures); (b) identification of all sites, including suppliers and sub-contractors, where manufacturing activities are performed.

4. GENERAL SAFETY AND PERFORMANCE REQUIREMENTS		General safety and performance requirements
The documentation shall contain information for the demonstration of conformity with the general safety and performance requirements set out in Annex I that are applicable to the device taking into account its intended purpose, and shall include a justification, validation and verification of the solutions adopted to meet those requirements. The demonstration of conformity shall also include: (a) the general safety and performance requirements that apply to the device and an explanation as to why others do not apply; (b) the method or methods used to demonstrate conformity with each applicable general safety and performance requirement; (c) the harmonised standards, CS or other solutions applied; (d) the precise identity of the controlled documents offering evidence of conformity with each harmonised standard, CS or other method applied to demonstrate conformity with the general safety and performance requirements. The information referred to under this point shall incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation.	As appropriate pointing to the appropriate part of either EU or UK legislation. Slight split in EU legislation to keep it aligned to UK legislation. Note harmonised standard versus designated standards.	5 .—(1) The documentation must contain information for the demonstration of conformity with the general safety and performance requirements set out in Schedule 17 that are applicable to the device taking into account its intended purpose, and must include a justification, validation and verification of the solutions adopted to meet those requirements. (2) The demonstration of conformity must also include— (a) the general safety and performance requirements that apply to the device and an explanation as to why others do not apply; (b) the method or methods used to demonstrate conformity with each applicable general safety and performance requirement; (c) the designated standards, CS or other solutions applied; (d) the precise identity of the controlled documents offering evidence of conformity with each designated standard, CS or other method applied to demonstrate conformity with the general safety and performance requirements. (e) the information referred to in paragraph (d) must incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation.

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5. BENFIT-RISK ANALYSIS AND RISK MANAGEMENT		Benefit-risk analysis and risk management
The documentation shall contain information on: (a) the benefit-risk analysis referred to in Sections 1 and 8 of Annex I, and (b) the solutions adopted and the results of the risk management referred to in Section 3 of Annex I.	As appropriate pointing to the appropriate part of either EU or UK legislation.	6. The documentation must contain information on— (a) the benefit-risk analysis referred to in paragraphs 1 and 8 of Schedule 17, (b) the solutions adopted and the results of the risk management referred to in paragraph 3 of Schedule 17.

6. PRODUCT VERIFICATION AND VALIDATION		Product verification and validation
The documentation shall contain the results and critical analyses of all verifications and validation tests and/or studies undertaken to demonstrate conformity of the device with the requirements of this Regulation and in particular the applicable general safety and performance requirements. This includes: 6.1. Information on analytical performance of the device 6.1.1. Specimen type This Section shall describe the different specimen types that can be analysed, including their stability such as storage, where applicable specimen transport conditions and, with a view to time-critical analysis methods, information on the timeframe between taking the specimen and its analysis and storage conditions such as duration, temperature limits and freeze/thaw cycles.	As appropriate pointing to the appropriate part of either EU or UK legislation. EU and UK legislation layout these requirements differently but they are the same.	7. The documentation must contain the results and critical analyses of all verifications and validation tests or studies undertaken to demonstrate conformity of the device with the requirements Part IX and Schedules 17 to 28 and in particular the applicable general safety and performance requirements in Schedule 17. 8.—(1) The documentation must include the information on the performance of the device listed in sub-paragraphs (2) and (3). (2) The specimen type which must describe the different specimen types that can be analysed, including their stability such as storage, where applicable specimen transport conditions and, with a view to time-critical analysis methods, information on the timeframe between taking the specimen and its analysis and storage conditions such as duration, temperature limits and freeze/thaw cycles;

6.1.2. Analytical performance characteristics		temperature limits and freeze/thaw cycles;
6.1.2.1. Accuracy of measurement		(3) The accuracy of the measurement consisting of—
(a) Trueness of measurement		
This Section shall provide information on the trueness of the measurement procedure and summarise the data in sufficient detail to allow an assessment of the adequacy of the means selected to establish the trueness. Trueness measures apply to both quantitative and qualitative assays only when a certified reference material or certified reference method is available.		(a) the trueness of the measurement which must provide information on the trueness of the measurement procedure and summarise the data in sufficient detail to allow an assessment of the adequacy of the means selected to establish the trueness whilst noting that trueness measures apply to both quantitative and qualitative assays only when a certified reference material or certified reference method is available;
(b) Precision of measurement		(b) the precision of the measurement which must describe the repeatability and reproducibility studies;
This Section shall describe repeatability and reproducibility studies.		
6.1.2.2. Analytical sensitivity		(c) the analytical sensitivity which must include—
This Section shall include information about the study design and results.	Slight split in EU legislation to keep it aligned to UK legislation.	(i) information about the study design and results;
It shall provide a description of specimen type and preparation including matrix, analyte levels, and how levels were established.		(ii) a description of specimen type and preparation including matrix, analyte levels, and how levels were established;
The number of replicates tested at each concentration shall also be provided as well as a description of the calculation used to determine assay sensitivity.		(ii) the number of replicates tested at each concentration must also be provided as well as a description of the calculation used to determine assay sensitivity;

6.1.2.3. Analytical specificity This Section shall describe interference and cross reactivity studies performed to determine the analytical specificity in the presence of other substances/agents in the specimen. Information shall be provided on the evaluation of potentially interfering and cross-reacting substances or agents on the assay, on the tested substance or agent type and its concentration, specimen type, analyte test concentration, and results. Interferents and cross-reacting substances or agents, which vary greatly depending on the assay type and design, could derive from exogenous or endogenous sources such as: (a) substances used for patient treatment such as medicinal products; (b) substances ingested by the patient such as alcohol, foods; (c) substances added during specimen preparation such as preservatives, stabilisers; (d) substances encountered in specific specimen types such as haemoglobin, lipids, bilirubin, proteins; (e) analytes of similar structure such as precursors, metabolites or medical conditions unrelated to the test condition including specimens negative for the assay but positive for a condition that can mimic the test condition.		(d) analytical specificity which must include— (i) a description of interference and cross reactivity studies performed to determine the analytical specificity in the presence of other substances/agents in the specimen; (ii) information on the evaluation of potentially interfering and cross-reacting substances or agents on the assay, on the tested substance or agent type and its concentration, specimen type, analyte test concentration, and results; (iii) information on interferents and cross-reacting substances or agents, which vary greatly depending on the assay type and design and could derive from exogenous or endogenous sources such as— (aa) substances used for patient treatment such as medicinal products; (bb) substances ingested by the patient such as alcohol, foods; (cc) substances added during specimen preparation such as preservatives, stabilisers; (dd) substances encountered in specific specimen types such as haemoglobin, lipids, bilirubin, proteins; (ee) analytes of similar structure such as precursors, metabolites or medical conditions unrelated to the test condition including specimens negative for the assay but positive for a condition that can mimic the test condition;

6.1.2.4. Metrological traceability of calibrator and control material values 6.1.2.5. Measuring range of the assay This Section shall include information on the measuring range regardless of whether the measuring systems are linear or non-linear, including the limit of detection and describe information on how the range and detection limit were established. This information shall include a description of specimen type, number of specimens, number of replicates, and specimen preparation including information on the matrix, analyte levels and how levels were established. If applicable, a description of any high dose hook effect and the data supporting the mitigation such as dilution steps shall be added. 6.1.2.6. Definition of assay cut-off This Section shall provide a summary of analytical data with a description of the study design including methods for determining the assay cut-off, such as: (a) the population(s) studied: demographics, selection, inclusion and exclusion criteria, number of individuals included; (b) method or mode of characterisation of specimens; and	Slight split in EU legislation to keep it aligned to UK legislation.	(iv) the metrological traceability of calibrator and control material values; (v) the measuring range of the assay which must include information— (vi) on the measuring range regardless of whether the measuring systems are linear or non-linear, including the limit of detection and describe information on how the range and detection limit were established; (vii) including a description of specimen type, number of specimens, number of replicates, and specimen preparation including information on the matrix, analyte levels and how levels were established; (viii) applicable, a description of any high dose hook effect and the data supporting the mitigation such as dilution steps shall be added; (ix) a definition of the assay cut-off including— (x) a summary of analytical data with a description of the study design including methods for determining the assay cut-off, such as— (aa) the populations studied including demographics, selection, inclusion and exclusion criteria, number of individuals included; (bb) the method or mode of characterisation of specimens;

(c) statistical methods such as Receiver Operator Characteristic (ROC) to generate results and if applicable, define grey-zone/equivocal zone. 6.1.3. The analytical performance report referred to in Annex XIII.	As appropriate pointing to the appropriate part of either EU or UK legislation.	(cc) statistical methods such as Receiver Operator Characteristic (ROC) to generate results and if applicable, define grey-zone/equivocal zone; (xi) the analytical performance report referred to in Schedule 27.

6.2. Information on clinical performance and clinical evidence. Performance Evaluation Report The documentation shall contain the performance evaluation report, which includes the reports on the scientific validity, the analytical and the clinical performance, as referred to in Annex XIII, together with an assessment of those reports. The clinical performance study documents referred to in Section 2 of Part A of Annex XIII shall be included and/or fully referenced in the technical documentation.	As appropriate pointing to the appropriate part of either EU or UK legislation.	9. The documentation— (a) must contain the performance evaluation report, which includes the reports on the scientific validity, the analytical and the clinical performance, as referred to in Schedule 27, together with an assessment of those reports; (b) must include, or fully reference, the clinical performance study documents referred to in paragraph 2 of Part A of Schedule 27.

6.3. Stability (excluding specimen stability) This Section shall describe claimed shelf life, in use stability and shipping stability studies. 6.3.1. Claimed shelf-life This Section shall provide information on stability testing studies to support the shelf life that is claimed for the device. Testing shall be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions. The three lots do not need to be consecutive. Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claims but shall be followed up with real time stability studies. Such detailed information shall include: (a) the study report including the protocol, number of lots, acceptance criteria and testing intervals; (b) where accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies shall be described; (c) the conclusions and claimed shelf life.		Shelf life, in-use stability and shipping stability studies 10. The documentation must describe claimed shelf life, in use stability and shipping stability studies. 11. For claimed shelf life the documentation must— (a) provide information on stability testing studies to support the shelf life that is claimed for the device; (b) confirm that testing has been performed on at least 3 different (but not necessarily consecutive) lots manufactured under conditions that are essentially equivalent to routine production conditions; (c) describe whether accelerated studies or extrapolated data from real time data are used for initial shelf life claims and that these studies will be followed up with real time stability studies; (d) include the detailed information in paragraphs (b) to (c) which must include— (i) the study report including the protocol, number of lots, acceptance criteria and testing intervals; (ii) where accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies must be described; (iii) the conclusions and claimed shelf life.

6.3.2. In-use stability This Section shall provide information on in-use stability studies for one lot reflecting actual routine use of the device, regardless of whether real or simulated. This may include open vial stability and/or, for automated instruments, on board stability. In the case of automated instrumentation, if calibration stability is claimed, supporting data shall be included. Such detailed information shall include: (a) the study report (including the protocol, acceptance criteria and testing intervals); (b) the conclusions and claimed in-use stability.		12. For in-use stability the documentation must— (a) provide information on in-use stability studies for one lot reflecting actual routine use of the device, regardless of whether real or simulated which may include open vial stability or, for automated instruments, on board stability; (b) provide supporting data in cases of automated instrumentation where calibration stability is claimed; (c) include— (i) the study report (including the protocol, acceptance criteria and testing intervals); (ii) the conclusions and claimed in-use stability.
6.3.3. Shipping stability This Section shall provide information on shipping stability studies for one lot of devices to evaluate the tolerance of devices to the anticipated shipping conditions. Shipping studies may be done under real and/or simulated conditions and shall include variable shipping conditions such as extreme heat and/or cold. Such information shall describe: (a) the study report (including the protocol, acceptance criteria); (b) the method used for simulated conditions; (c) the conclusion and recommended shipping conditions.		13. For shipping stability the documentation must— (a) provide information on shipping stability studies for one lot of devices to evaluate the tolerance of devices to the anticipated shipping conditions; (b) provide information on whether the shipping studies were done under real or simulated conditions and must include variable shipping conditions such as extreme heat and/or cold; (c) include— (i) the study report (including the protocol, acceptance criteria); (ii) the method used for simulated conditions; (iii) conclusion and recommended shipping conditions.

6.4. Software verification and validation The documentation shall contain evidence of the validation of the software, as it is used in the finished device. Such information shall typically include the summary results of all verification, validation and testing performed in-house and applicable in an actual user environment prior to final release. It shall also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling	Slight split in EU legislation to keep it aligned to UK legislation.	Software verification and validation 14. The documentation must— (a) contain evidence of the validation of the software, as it is used in the finished device; (b) typically include the summary results of all verification, validation and testing performed in-house and applicable in an actual user environment prior to final release; (c) also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling.

6.5. Additional information required in specific cases (a) In the case of devices placed on the market in a sterile or defined microbiological condition, a description of the environmental conditions for the relevant manufacturing steps. In the case of devices placed on the market in a sterile condition, a description of the methods used, including the validation reports, with regard to packaging, sterilisation and maintenance of sterility. The validation report shall address bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues. (b) In the case of devices containing tissues, cells and substances of animal, human or microbial origin, information on the origin of such material and on the conditions in which it was collected. (c) In the case of devices placed on the market with a measuring function, a description of the methods used in order to ensure the accuracy as given in the specifications. (d) If the device is to be connected to other equipment in order to operate as intended, a description of the resulting combination including proof that it conforms to the general safety and performance requirements set out in Annex I when connected to any such equipment having regard to the characteristics specified by the manufacturer.	Slight split in EU legislation to keep it aligned to UK legislation.	Additional information required in specific cases 15. The additional information required in specific cases is as follows— (a) in the case of devices placed on the market in a sterile or defined microbiological condition, a description of the environmental conditions for the relevant manufacturing steps; (b) in the case of devices placed on the market in a sterile condition, a description of the methods used, including the validation reports, with regard to packaging, sterilisation and maintenance of sterility and the validation report must address bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues; (c) in the case of devices containing tissues, cells and substances of animal, human or microbial origin, information on the origin of such material and on the conditions in which it was collected; (d) in the case of devices placed on the market with a measuring function, a description of the methods used in order to ensure the accuracy as given in the specifications; (e) if the device is to be connected to other equipment in order to operate as intended, a description of the resulting combination including proof that it conforms to the general safety and performance requirements set out in Schedule 17 when connected to any such equipment having regard to the characteristics specified by the manufacturer.

ANNEX III - TECHNICAL DOCUMENTATION ON POST-MARKET SURVEILLANCE		SCHEDULE 19 Regulation 1A - Technical documentation on post-market surveillance for in vitro diagnostic medical devices
The technical documentation on post-market surveillance to be drawn up by the manufacturer in accordance with Articles 78 to 81 shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular the elements described in this Annex.	As appropriate pointing to the appropriate part of either EU or UK legislation.	1. The technical documentation on post-market surveillance to be drawn up by the manufacturer in accordance with regulations 186 to 189 must be presented in a clear, organised, readily searchable and unambiguous manner and must include in particular the elements described in this Schedule.
1. The post-market surveillance plan drawn up in accordance with Article 79. The manufacturer shall prove in a post-market surveillance plan that it complies with the obligation referred to in Article 78. (a) The post-market surveillance plan shall address the collection and utilisation of available information, in particular: — information concerning serious incidents, including information from periodic safety update report ('PSUR'), and field safety corrective actions, — records referring to non-serious incidents and data on any undesirable side-effects, — information from trend reporting, — relevant specialist or technical literature, databases and/or registers, — information, including feedbacks and complaints, provided by users, distributors and importers, and — publicly-available information about similar medical devices.	As appropriate pointing to the appropriate part of either EU or UK legislation. Slight split in EU legislation to keep it aligned to UK legislation.	2. In the post market surveillance plan drawn up in accordance with regulation 187 the manufacturer must prove that the plan complies with the obligation in regulation 186. 3. The post-market surveillance plan must address the collection and utilisation of available information, in particular— (a) information concerning serious incidents, including information from periodic safety update report ('PSUR'), and field safety corrective actions; (b) records referring to non-serious incidents and data on any undesirable side-effects, (c) information from trend reporting; (d) relevant specialist or technical literature, databases and/or registers; (e) information, including feedbacks and complaints, provided by users, distributors and importers; (f) publicly-available information about similar medical devices.

(b) The post-market surveillance plan shall cover at least: — a proactive and systematic process to collect any information referred to in point (a). The process shall allow a correct characterisation of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market; — effective and appropriate methods and processes to assess the collected data; — suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I; — effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field; — methods and protocols to manage the events subject to the trend report as provided for in Article 83, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period; — methods and protocols to communicate effectively with competent authorities, notified bodies, economic operators and users; — reference to procedures to fulfil the manufacturers obligations laid down in Articles 78, 79 and 81; — systematic procedures to identify and initiate appropriate measures including corrective actions;	As appropriate pointing to the appropriate part of either EU or UK legislation.	4. The post-market surveillance plan must cover at least— (a) a proactive and systematic process to collect any information referred to in paragraph 3 which must allow a correct characterisation of the performance of the devices and must also allow a comparison to be made between the device and similar products available on the market; (b) effective and appropriate methods and processes to assess the collected data; (c) suitable indicators and threshold values that must be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in paragraph 3 of Schedule 3; (d) effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field; (e) methods and protocols to manage the events subject to the trend report as provided for in regulation 191, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period; (f) methods and protocols to communicate effectively with the Secretary of State, notified bodies, economic operators and users; (g) reference to procedures to fulfil the manufacturers obligations laid down in regulations 186, 187 and 189; (h) systematic procedures to identify and initiate appropriate measures including corrective actions;

— effective tools to trace and identify devices for which corrective actions might be necessary; and — a PMPF plan as referred to in Part B of Annex XIII, or a justification as to why a PMPF is not applicable.		(i) effective tools to trace and identify devices for which corrective actions might be necessary; and (j) PMPF plan as referred to in Part B of Schedule 27 or a justification as to why a PMPF is not applicable.
2. The PSUR referred to in Article 81 and the post-market surveillance report referred to in Article 80.		5. The PSUR referred to in Article 81 and the post-market surveillance report referred to in Article 80.

PSUR - Periodic Safety Update Report
PMPF - Post-Market Performance Follow-up
PMCF – Post Market clinical Follow-up

For Medical Devices

Medical Device Regulation MDR REGULATION (EU) 2017/746 Annex II and Annex III		2019 No. 791 Exiting the European Union Consumer Protection, The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 Schedule 4 and Schedule 5 of the act.
TECHNICAL DOCUMENTATION The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular the elements listed in this Annex. *(II)*	Pointing to appropriate parts of the legislation.	SCHEDULE 4 Regulation 1A Technical Documentation 1. The technical documentation and, if applicable, the summary of that documentation drawn up by the manufacturer must be presented in clear, organised, readily searchable and unambiguous manner and must include the elements listed in this Schedule. *(4)*
1. Device description and specification including, variants and accessories		Device description and specification including variants and accessories
1.1. Device description and specification (a) product or trade name and a general description of the device including its intended purpose and intended users; (b) the Basic UDI-DI as referred to in Part C of Annex VI assigned by the manufacturer to the device in question, as soon as identification of this device becomes based on a UDI system, or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability; (c) the intended patient population and medical conditions to be diagnosed, treated and/or monitored and other considerations such as patient selection criteria, indications, contra-indications, warnings; (d) principles of operation of the device and its mode of action, scientifically demonstrated if necessary;	Pointing to appropriate parts of the legislation.	Device description and specification 2.—(1) The description and specification of a device must contain the following— (a) the product or trade name and a general description of the device including its intended purpose and intended users; (b) the Basic UDI-DI as referred to in Part C of Schedule 8 assigned by the manufacturer to the device in question, as soon as identification of this device becomes based on a UDI system, or otherwise a clear identification by means of product code, catalogue number or other unambiguous reference allowing traceability; (c) the intended patient population and medical conditions to be diagnosed, treated or monitored and other considerations such as patient selection criteria, indications, contra-indications, warnings; (d) principles of operation of the device and its mode of action, scientifically demonstrated if necessary;

(e) the rationale for the qualification of the product as a device;		(e) the rationale for the qualification of the product as a device;

(f) the risk class of the device and the justification for the classification rule(s) applied in accordance with Annex VIII; (g) an explanation of any novel features; (h) a description of the accessories for a device, other devices and other products that are not devices, which are intended to be used in combination with it; (i) a description or complete list of the various configurations/variants of the device that are intended to be made available on the market; (j) a general description of the key functional elements, e.g. its parts/components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition. Where appropriate, this shall include labelled pictorial representations (e.g. diagrams, photographs, and drawings), clearly indicating key parts/components, including sufficient explanation to understand the drawings and diagrams; (k) a description of the raw materials incorporated into key functional elements and those making either direct contact with the human body or indirect contact with the body, e.g., during extracorporeal circulation of body fluids;	Pointing to the appropriate part of either EU or UK legislation. Point (j) in EU legislation has been divided up to align with the UK legislation	(f) the risk class of the device and the justification for the classification rules applied in accordance with Schedule 9; (g) an explanation of any novel features; (h) a description of the accessories for the device, other devices and other products that are not devices, which are intended to be used in combination with it; (i) a description or complete list of the various configurations or variants of the device that are intended to be made available on the market; (j) a general description— (i) of the key functional elements, for example its parts or components (including software if appropriate), its formulation, its composition, its functionality and, where relevant, its qualitative and quantitative composition; and (ii) which, where appropriate, must include labelled pictorial representations (for example diagrams, photographs, and drawings), clearly indicating key parts or components, including sufficient explanation to understand the drawings and diagrams; (k) a description of the raw materials incorporated into key functional elements and those making either direct contact with the human body or indirect contact with the body, for example during extracorporeal circulation of body fluids;

(l) technical specifications, such as features, dimensions and performance attributes, of the device and any variants/configurations and accessories that would typically appear in the product specification made available to the user, for example in brochures, catalogues and similar publications.		(l) technical specifications, such as features, dimensions and performance attributes, of the device and any variants or configurations and accessories that would typically appear in the product specification made available to the user, for example in brochures, catalogues and similar publications.
1.2. Reference to previous and similar generations of the device (a) an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist; (b) an overview of identified similar devices available on the Union or international markets, where such devices exist.		Reference to previous and similar generations of the device (2) Where applicable the technical documentation must contain— (a) an overview of the previous generation or generations of the device produced by the manufacturer, where such devices exist; (b) an overview of identified similar devices available on the international markets, where such devices exist.

2. Information to be supplied by the manufacturer		Information to be supplied by the manufacturer
A complete set of: - the label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in case of specific management conditions, in the languages accepted in the Member States where the device is envisaged to be sold; and - the instructions for use in the languages accepted in the Member States where the device is envisaged to be sold.	UK only needs English	3. The manufacturer must supply a complete set of— (a) the label or labels on the device and on its packaging, such as single unit packaging, sales packaging, transport packaging in case of specific management conditions in English; and (b) the instructions for use in English.

3. DESIGN AND MANUFACTURING INFORMATION		Design and manufacturing information
(a) information to allow the design stages applied to the device to be understood; (b) complete information and specifications, including the manufacturing processes and their validation, their adjuvants, the continuous monitoring and the final product testing. Data shall be fully included in the technical documentation; (c) identification of all sites, including suppliers and sub-contractors, where design and manufacturing activities are performed.	The wording between the two is different but in the end is the same requirement. But for both remember to detail activities, location and control of subcontract work as required by BS EN 13485.	4. The following design and manufacturing information must be supplied— (a) information (including full data) to allow the design stages applied to the device to be understood; (b) complete information (including full data) and specifications, including the manufacturing processes and their validation, their adjuvants, the continuous monitoring and the final product testing.

4. General safety and performance requirements		General safety and performance requirements
The documentation shall contain information for the demonstration of conformity with the general safety and performance requirements set out in Annex I that are applicable to the device taking into account its intended purpose, and shall include a justification, validation and verification of the solutions adopted to meet those requirements. The demonstration of conformity shall include: (a) the general safety and performance requirements that apply to the device and an explanation as to why others do not apply; (b) the method or methods used to demonstrate conformity with each applicable general safety and performance requirement; (c) the harmonised standards, CS or other solutions applied; and (d) the precise identity of the controlled documents offering evidence of conformity with each harmonised standard, CS or other method applied to demonstrate conformity with the general safety and performance requirements. The information referred to under this point shall incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation.	Pointing to the appropriate part of either EU or UK legislation. Must check for 'other solutions' - UK or 'CS' – EU. These might differ in the future.	5.—(1) The documentation must contain information for the demonstration of conformity with the general safety and performance requirements set out in Schedule 3 that are applicable to the device taking into account its intended purpose, and must include a justification, validation and verification of the solutions adopted to meet those requirements. (2) The demonstration of conformity in sub-paragraph (1) must include— (a) the general safety and performance requirements that apply to the device and an explanation as to why others do not apply; (b) the method or methods used to demonstrate conformity with each applicable general safety and performance requirement; (c) the standards or other solutions applied; (d) the precise identity of the controlled documents offering evidence of conformity with each standard, or other method applied to demonstrate conformity with the general safety and performance requirements; and (e) the information referred to paragraph (d) must incorporate a cross-reference to the location of such evidence within the full technical documentation and, if applicable, the summary technical documentation.

CS - common specifications

5. Benefit-risk analysis and risk management		Benefit-risk analysis and risk management

The documentation shall contain information on: (a) the benefit-risk analysis referred to in Sections 1 and 8 of Annex I, and (b) the solutions adopted and the results of the risk management referred to in Section 3 of Annex I.	Pointing to the appropriate part of either EU or UK legislation.	6. The technical documentation must contain information on— (a) the benefit-risk analysis referred to in paragraphs 1 and 8 of Schedule 3; (b) the solutions adopted and the results of the risk management referred to in paragraph 3 of Schedule 3.

6. PRODUCT VERIFICATION AND VALIDATION		Product verification and validation
The documentation shall contain the results and critical analyses of all verifications and validation tests and/or studies undertaken to demonstrate conformity of the device with the requirements of this Regulation and in particular the applicable general safety and performance requirements. 6.1. Pre-clinical and clinical data (a) results of tests, such as engineering, laboratory, simulated use and animal tests, and evaluation of published literature applicable to the device, taking into account its intended purpose, or to similar devices, regarding the pre-clinical safety of the device and its conformity with the specifications; (b) detailed information regarding test design, complete test or study protocols, methods of data analysis, in addition to data summaries and test conclusions regarding in particular: - the biocompatibility of the device including the identification of all materials in direct or indirect contact with the patient or user; - physical, chemical and microbiological characterisation; - electrical safety and electromagnetic compatibility;	Pointing to the appropriate part of either EU or UK legislation.	Product verification and validation 7.—(1) The documentation must contain the results and critical analyses of all verifications and validation tests or studies undertaken to demonstrate conformity of the device with the requirements of Part VIII and in particular the applicable general safety and performance requirements. Pre-clinical and clinical data. (2) The documentation must contain the following pre-clinical and clinical data— (a) results of tests, such as engineering, laboratory, simulated use and animal tests, and evaluation of published literature applicable to the device, taking into account its intended purpose, or to similar devices, regarding the pre-clinical safety of the device and its conformity with the specifications; (b) detailed information regarding test design, complete test or study protocols, methods of data analysis, in addition to data summaries and test conclusions regarding in particular— (i) the biocompatibility of the device including the identification of all materials in direct or indirect contact with the patient or user; (ii) physical, chemical and microbiological characterisation; (iii)electrical safety and electromagnetic compatibility;

- software verification and validation (describing the software design and development process and evidence of the validation of the software, as used in the finished device. This information shall typically include the summary results of all verification, validation and testing performed both in-house and in a simulated or actual user environment prior to final release. It shall also address all of the different hardware configurations and, where applicable, operating systems identified in the information supplied by the manufacturer); - stability, including shelf life; and - performance and safety. Where applicable, conformity with the provisions of Directive 2004/10/EC of the European Parliament and of the Council (1) shall be demonstrated. Where no new testing has been undertaken, the documentation shall incorporate a rationale for that decision. An example of such a rationale would be that biocompatibility testing on identical materials was conducted when those materials were incorporated in a previous version of the device that has been legally placed on the market or put into service; (	This para in EU legislation has been divided up to align with the UK legislation Pointing to EU or UK legislation as required.	(iv) software verification and validation which must— (aa) describe the software design and development process and provide evidence of the validation of the software, as used in the finished device; (bb) typically include the summary results of all verification, validation and testing performed both in-house and in a simulated or actual user environment prior to final release; and (cc) address all of the different hardware configurations and, where applicable, operating systems identified in the information supplied by the manufacturer; (v) stability, including shelf life; and (vi) performance and safety. (3) Where applicable, conformity with the Good Laboratory Practice Regulations 1999(a) must be demonstrated. (4) Where no new testing has been undertaken, the documentation must incorporate a rationale for that decision (for example, a rationale would be that biocompatibility testing on identical materials was conducted when those materials were incorporated in a previous version of the device that has been legally placed on the market or put into service).

c) the clinical evaluation report and its updates and the clinical evaluation plan referred to in Article 61(12) and Part A of Annex XIV; (d) the PMCF plan and PMCF evaluation report referred to in Part B of Annex XIV or a justification why a PMCF is not applicable.	Pointing to the appropriate part of either EU or UK legislation.	(5) The documentation must also include— (a) the clinical evaluation report and its updates and the clinical evaluation plan referred to in regulation 102(14) and Part A of Schedule 14; (b) the PMCF plan and PMCF evaluation report referred to in Part B of Schedule 14 or a justification why a PMCF is not applicable.

PMCF - POST-MARKET CLINICAL FOLLOW-UP

6.2. Additional information required in specific cases (a) Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma, as referred to in the first subparagraph of Article 1(8), a statement indicating this fact. In this case, the documentation shall identify the source of that substance and contain the data of the tests conducted to assess its safety, quality and usefulness, taking account of the intended purpose of the device. (b) Where a device is manufactured utilising tissues or cells of human or animal origin, or their derivatives, and is covered by this Regulation in accordance with points (f) and (g) of Article 1(6, and where a device incorporates, as an integral part, tissues or cells of human origin or their derivatives that have an action ancillary to that of the device and is covered by this Regulation in accordance with the first subparagraph of Article 1(10), a statement indicating this fact. In such a case, the documentation shall identify all materials of human or animal origin used and provide detailed information concerning the conformity with Sections 13.1. or 13.2., respectively, of Annex I.	Various paragraphs in EU legislation has been divided up to align with the UK legislation Also pointing to the appropriate part of either EU or UK legislation.	Additional information required in specific cases (6) The additional information specified is required as part of the technical documentation in the following cases— (a) where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of regulation 2(1) of the Human Medicines Regulations 2012 including a medicinal product derived from human blood or human plasma, as referred to in regulation 68(8)— (i) a statement indicating this fact; and (ii) documentation sufficient to identify the source of that substance and contain the data of the tests conducted to assess its safety, quality and usefulness, taking account of the intended purpose of the device; (b) where a device is manufactured utilising tissues or cells of human or animal origin, or their derivatives, and is covered by Part VIII in accordance with sub-paragraphs (g) and (h) of regulation 68(6), and where a device incorporates, as an integral part, tissues or cells of human origin or their derivatives that have an action ancillary to that of the device and is covered by Part VIII in accordance with regulation 68(14), (i) a statement indicating this fact; and (ii) documentation sufficient to identify all materials of human or animal origin used and provide detailed information concerning the conformity with sub- paragraphs (1) and (2) of paragraph 13 of Schedule 3;

(c) In the case of devices that are composed of substances or combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body, detailed information, including test design, complete test or study protocols, methods of data analysis, and data summaries and test conclusions, regarding studies in relation to: - absorption, distribution, metabolism and excretion; - possible interactions of those substances, or of their products of metabolism in the human body, with other devices, medicinal products or other substances, considering the target population, and its associated medical conditions; - local tolerance; and - toxicity, including single-dose toxicity, repeat-dose toxicity, genotoxicity, carcinogenicity and reproductive and developmental toxicity, as applicable depending on the level and nature of exposure to the device. In the absence of such studies, a justification shall be provided. (d) In the case of devices containing CMR or endocrine-disrupting substances referred to in Section 10.4.1 of Annex I, the justification referred to in Section 10.4.2 of that Annex.	Pointing to the appropriate part of either EU or UK legislation.	(c) in the case of devices that are composed of substances or combinations of substances that are intended to be introduced into the human body and that are absorbed by or locally dispersed in the human body, detailed information, including test design, complete test or study protocols, methods of data analysis, and data summaries and test conclusions, regarding studies in relation to— (i) absorption, distribution, metabolism and excretion; (ii) possible interactions of those substances, or of their products of metabolism in the human body, with other devices, medicinal products or other substances, considering the target population, and its associated medical conditions; (iii) local tolerance; (iv) toxicity, including single-dose toxicity, repeat-dose toxicity, genotoxicity, carcinogenicity and reproductive and developmental toxicity, as applicable depending on the level and nature of exposure to the device and in the absence of such studies, a justification shall be provided; (d) in the case of devices containing CMR or endocrine-disrupting substances referred to in paragraph 10(7) of Schedule 3, the justification referred to in paragraph 10(9) of that Schedule;

(e) In the case of devices placed on the market in a sterile or defined microbiological condition, a description of the environmental conditions for the relevant manufacturing steps. In the case of devices placed on the market in a sterile condition, a description of the methods used, including the validation reports, with respect to packaging, sterilisation and maintenance of sterility. The validation report shall address bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues. (f) In the case of devices placed on the market with a measuring function, a description of the methods used in order to ensure the accuracy as given in the specifications. (g) If the device is to be connected to other device(s) in order to operate as intended, a description of this combination/configuration including proof that it conforms to the general safety and performance requirements when connected to any such device(s) having regard to the characteristics specified by the manufacturer.	Point (e) in EU legislation has been divided up to align with the UK legislation.	(e) in the case of devices placed on the market in a sterile or defined microbiological condition, a description of the environmental conditions for the relevant manufacturing steps; (f) in the case of devices placed on the market in a sterile condition— (i) a description of the methods used; and (ii) validation reports, with respect to packaging, sterilisation and maintenance of sterility which must address bioburden testing, pyrogen testing and, if applicable, testing for sterilant residues; (g) in the case of devices placed on the market with a measuring function, a description of the methods used in order to ensure the accuracy as given in the specifications; (h) if the device is to be connected to other devices in order to operate as intended, a description of this combination or configuration including proof that it conforms to the general safety and performance requirements when connected to any such devices having regard to the characteristics specified by the manufacturer.

ANNEX III - Technical documentation on post-market surveillance		SCHEDULE 5Regulation 1A - Technical documentation on post-market surveillance
The technical documentation on post-market surveillance to be drawn up by the manufacturer in accordance with Articles 83 to 86 shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include in particular the elements described in this Annex. 1.1. The post-market surveillance plan drawn up in accordance with Article 84. The manufacturer shall prove in a post-market surveillance plan that it complies with the obligation referred to in Article 83. (a) The post-market surveillance plan shall address the collection and utilization of available information, in particular: - information concerning serious incidents, including information from PSURs, and field safety corrective actions; - records referring to non-serious incidents and data on any undesirable side-effects; - information from trend reporting; - relevant specialist or technical literature, databases and/or registers; - information, including feedbacks and complaints, provided by users, distributors and importers; and - publicly available information about similar medical devices.	Also pointing to the appropriate part of either EU or UK legislation. This is not present in the UK legislation.	1.—(1) The technical documentation on post-market surveillance drawn up by the manufacturer in accordance with regulations 121 to 123 must be presented in a clear, organised, readily searchable and unambiguous manner and must include in particular the elements described in sub-paragraphs (2) to (4) this Schedule. (2) In the post-market surveillance plan drawn up in accordance with regulation 122, the manufacturer must prove that the requirements of regulation 121 have been met. (3) The post-market surveillance plan must— (a) address the collection and utilization of available information, in particular— (i) information concerning serious incidents, including information from PSURs, and field safety corrective actions; (ii) records referring to non-serious incidents and data on any undesirable side- effects; (iii) information from trend reporting; (iv) information, including feedbacks and complaints, provided by users, distributors and importers; (v) publicly available information about similar medical devices;

(b) The post-market surveillance plan shall cover at least:		(b) cover at least—

- a proactive and systematic process to collect any information referred to in point (a). The process shall allow a correct characterisation of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market; - effective and appropriate methods and processes to assess the collected data; - suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I; - effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field; - methods and protocols to manage the events subject to the trend report as provided for in Article 88, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period;	Pointing to the appropriate part of either EU or UK legislation in various parts.	(i) a proactive and systematic process to collect any information referred to in sub-paragraph 1(2). The process must allow a correct characterisation of the performance of the devices and must also allow a comparison to be made between the device and similar products available on the market; (ii) effective and appropriate methods and processes to assess the collected data; (iii) suitable indicators and threshold values that must be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in paragraph 3 of Schedule 3; (iv) effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field; (v) methods and protocols to manage the events subject to the trend report as provided for in regulation 126, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period; (

- methods and protocols to communicate effectively with competent authorities, notified bodies, economic operators and users; - reference to procedures to fulfil the manufacturers obligations laid down in Articles 83, 84 and 86; - systematic procedures to identify and initiate appropriate measures including corrective actions; - effective tools to trace and identify devices for which corrective actions might be necessary; and - a PMCF plan as referred to in Part B of Annex XIV, or a justification as to why a PMCF is not applicable. 1.2. The PSUR referred to in Article 86 and the post-market surveillance report referred to in Article 85.	Pointing to the appropriate part of either EU or UK legislation in various parts.	vi) methods and protocols to communicate effectively to the Secretary of State, economic operators and users; (vii) reference to procedures to fulfil the manufacturers obligations laid down in regulations 121, 122 and 124; (viii) systematic procedures to identify and initiate appropriate measures including corrective actions; (ix) effective tools to trace and identify devices for which corrective actions might be necessary; (x) a PMCF plan as referred to in Part B of Schedule 14, or a justification as to why a PMCF is not applicable. (4) The PSUR referred to in regulation 124 and the post-market surveillance report referred to in regulation 123.

PSUR - Periodic Safety Update Report
PMPF - Post-Market Performance Follow-up
PMCF – Post Market Clinical Follow-up.

Appendix C4 6 Comparisons of the requirements of all three sets of legislation hazard and risk – IVDR with MDR with UK Law:

The review of the differences between the risk management requirements of the MDR and the IVDR and then to compare these to the UK requirements
This review will include determining if any definitions given or requirements relating to risk management are the same. If not highlight these so that any QA documentation relating to risk management reflects these differences.

Note the comparison of the EU legislation was been carried out using the consolidated text of the regulations given at
1. MDR with consolidated text from 2019 - https://eur-lex.europa.eu/eli/reg/2017/745/2017-05-05 and using the PDF version of the text.
2. IVDR with consolidated text from 2019 https://eur-lex.europa.eu/eli/reg/2017/746/2017-05-05 and using the PDF version of the text.

   Both of these documents and also be found by following the links given in from the EU page
   https://ec.europa.eu/growth/sectors/medical-devices/new-regulations_en 'New regulations' which gives summary details of the new regulations.

The UK legislation used to compare the UK and EU legislation used the above EU legislation and the following UK legislation:
https://www.legislation.gov.uk/uksi/2019/791/contents/made

The main problem is the different way of referencing the requirements in the two EU regulations and the one UK statutory instrument..

PSUR - Periodic Safety Update Report
PMPF - Post Market Performance Follow-up
PMCF – Post Market clinical Follow-up
Application of Parts II and III on and after 26th May 2020, the related transitional provisions and the revocation of Parts II and III on 26th May 2025
4F.(7) The requirements of Part VIII in respect of post-market surveillance, market surveillance, vigilance and registration of economic operators and of devices apply in place of the corresponding requirements of Parts II and III (although regulations 7A and 21A may continue to apply, subject to paragraphs (3) and (4)). Need to look at this transition point in detail to figure out what it actually means,

The columns headings are:

IVDR	Comparison IVDR to MDR	MDR	Comparison MDR TO UK	UK

If the MDR and IVDR are then same then the comparison MDR to UK is valid for both.
IF the either the MDR or IVDR clauses are not shown then the comparison MDR to UK is for the relevant clause showing – MDR or IVDR..

CHAPTER I INTRODUCTORY PROVISIONS		CHAPTER I SCOPE AND DEFINITIONS		PART VIII Scope and Definitions
		Article 1 Subject matter and scope 2. This Regulation shall also apply, as from the date of application of common specifications adopted pursuant to Article 9, to the groups of products without an intended medical purpose that are listed in Annex XVI, taking into account the state of the art, and in particular existing harmonised standards for analogous devices with a medical purpose, based on similar technology. The common specifications for each of the groups of products listed in Annex XVI shall address, at least, application of risk management as set out in Annex I for the group of products in question and, where necessary, clinical evaluation regarding safety.		
CHAPTER II MAKING AVAILABLE ON THE MARKET AND PUTTING INTO SERVICE OF DEVICES, OBLIGATIONS OF ECONOMIC OPERATORS, CE MARKING, FREE MOVEMENT		CHAPTER II MAKING AVAILABLE ON THE MARKET AND PUTTING INTO SERVICE OF DEVICES, OBLIGATIONS OF ECONOMIC OPERATORS, REPROCESSING, CE MARKING, FREE MOVEMENT		
Article 8 Use of harmonised standards 1. Devices that are in conformity with the relevant harmonised standards, or the relevant parts of those standards, the references of which have been published in the Official Journal of the European Union, shall be presumed to be in conformity with the requirements of this Regulation covered by those standards or parts thereof. The first subparagraph shall also apply to system or process requirements to be fulfilled in accordance with this Regulation by economic operators or sponsors, including those relating to quality management systems, risk management, post-market surveillance systems, performance studies, clinical evidence or post-market performance follow-up ("PMPF").		Article 8 Use of harmonised standards 1. Devices that are in conformity with the relevant harmonised standards, or the relevant parts of those standards, the references of which have been published in the Official Journal of the European Union, shall be presumed to be in conformity with the requirements of this Regulation covered by those standards or parts thereof. The first subparagraph shall also apply to system or process requirements to be fulfilled in accordance with this Regulation by economic operators or sponsors, including those relating to quality management systems, risk management, post-market surveillance systems, clinical investigations, clinical evaluation or post-market clinical follow-up ("PMCF")		Use of designated standards 74.—(1) Devices that are in conformity with the designated standards, or the relevant parts of those standards, are presumed to be in conformity with the requirements of this Part covered by those standards or relevant parts of those standards. (2) Paragraph (1) also applies to system or process requirements to be fulfilled in accordance with this Part by economic operators or sponsors, including those relating to quality management systems, risk management, post-market surveillance systems, clinical investigations, clinical evaluation or post-market clinical follow-up ("PMCF").
Article 10 General obligations of manufacturers 2. Manufacturers shall establish, document, implement and maintain a system for risk management as described in Section 3 of Annex I. 8 . . . . The quality management system shall address at least the following aspects: (e) risk management as set out in Section 3 of Annex I;		Article 10 General obligations of manufacturers 2. Manufacturers shall establish, document, implement and maintain a system for risk management as described in Section 3 of Annex I. 9 . . . . . The quality management system shall address at least the following aspects: (e) risk management as set out in in Section 3 of Annex I;		General obligations of manufacturers 76. (2) Manufacturers must establish, document, implement and maintain a system for risk management as described in paragraph 3 of Schedule 3. (14) The quality management system required by paragraph (13) must— (c) provide details of at least the following— (v) risk management as set out in paragraph 3 of Schedule 3;

N/A		Article 17 Single-use devices and their reprocessing 1. Reprocessing and further use of single-use devices may only take place where permitted by national law and only in accordance with this Article. 2. Any natural or legal person who reprocesses a single-use device to make it suitable for further use within the Union shall be considered to be the manufacturer of the reprocessed device and shall assume the obligations incumbent on manufacturers laid down in this Regulation, which include obligations relating to the traceability of the reprocessed device in accordance with Chapter III of this Regulation. The reprocessor of the device shall be considered to be a producer for the purpose of Article 3(1) of Directive 85/374/EEC. 3. By way of derogation from paragraph 2., as regards single-use devices that are reprocessed and used within a health institution, Member States may decide not to apply all of the rules relating to manufacturers' obligations laid down in this Regulation provided that they ensure that: (a) the safety and performance of the reprocessed device is equivalent to that of the original device and the requirements in points (a), (b), (d), (e), (f), (g) and (h) of Article 5(5) are complied with; (b) the reprocessing is performed in accordance with CS detailing the requirements concerning: —risk management, including the analysis of the construction and material, related properties of the device (reverse engineering) and procedures to detect changes in the design of the original device as well as of its planned application after reprocessing, —the validation of procedures for the entire process, including cleaning steps, —the product release and performance testing, —the quality management system, —the reporting of incidents involving devices that have been reprocessed, and —the traceability of reprocessed devices. Member States shall encourage, and may require, health institutions to provide information to patients on the use of reprocessed devices within the health institution and, where appropriate, any other relevant information on the reprocessed devices that patients are treated with.		Single-use devices and their reprocessing 8[2].—(1) Reprocessing and further use of single-use devices may only take place in accordance with this Part. (2) Subject to paragraph (4), any person who reprocesses a single-use device to make it suitable for further use must be considered a manufacturer of the reprocessed device and must assume the obligations of a manufacturer in this Part. (3) A person who reprocesses a device must be considered to be the producer for the purposes of Part I of the 1987 Act. (4) Where single-use devices are reprocessed and used within a health institution, the Secretary of State may direct that not all the rules relating to manufacturers' obligations laid down in this Part apply provided that the following conditions are met— (a) the safety and performance of the reprocessed device is equivalent to that of the original device and the requirements of regulation 7[1](5) are complied with; (b) the reprocessing is performed in accordance with the CS detailing requirements concerning— (i) risk management, including the analysis of the construction and material, related properties of the device (reverse engineering) and procedures to detect changes in the design of the original device as well as of its planned application after reprocessing; (ii) the validation of procedures for the entire process, including cleaning steps; (iii) the product release and performance testing; (iv) the quality management system; (v) the reporting of incidents involving devices that have been reprocessed; and (vi) the traceability of reprocessed devices. (5) The Secretary of State must encourage and may require health institutions to provide information to patients on the use of reprocessed devices within the health institution and, where appropriate, any other information on the reprocessed devices that patients are treated with.	

		CHAPTER VI CLINICAL EVALUATION AND CLINICAL INVESTIGATIONS Article 61 Clinical evaluation 10. Without prejudice to paragraph 4, where the demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate, adequate justification for any such exception shall be given based on the results of the manufacturer's risk management and on consideration of the specifics of the interaction between the device and the human body, the clinical performance intended and the claims of the manufacturer. In such a case, the manufacturer shall duly substantiate in the technical documentation referred to in Annex II why it considers a demonstration of conformity with general safety and performance requirements that is based on the results of non-clinical testing methods, alone, including performance evaluation, bench testing and pre-clinical evaluation, to be adequate.		Clinical evaluation and clinical investigations Clinical evaluation (12) Without prejudice to paragraph (5), where the demonstration of conformity with general safety and performance requirements based on clinical data is not deemed appropriate, adequate justification for any such exception— (a) must be given based on the results of the manufacturer's risk management and on consideration of the specifics of the interaction between the device and the human body, the clinical performance intended and the claims of the manufacturer;

CHAPTER VII POST-MARKET SURVEILLANCE, VIGILANCE AND MARKET SURVEILLANCE Section 1 Post–market surveillance Article 78 Post-market surveillance system of the manufacturer 3. Data gathered by the manufacturer's post-market surveillance system shall in particular be used: (a) to update the benefit-risk determination and to improve the risk management as referred to in Chapter I of Annex I;		CHAPTER VII POST-MARKET SURVEILLANCE, VIGILANCE AND MARKET SURVEILLANCE SECTION 1 Post-market surveillance Article 83 Post-market surveillance system of the manufacturer 3. Data gathered by the manufacturer's post-market surveillance system shall in particular be used: (a) to update the benefit-risk determination and to improve the risk management as referred to in Chapter I of Annex I;		POST-MARKET SURVEILLANCE, VIGILANCE AND MARKET SURVEILLANCE Post-market surveillance Post-market surveillance system of the manufacturer (3) The manufacturer must ensure that— (a) data gathered by the manufacturer's post-market surveillance system is used in particular— (i) to update the benefit-risk determination and to improve the risk management as referred to in Part 1 of Schedule 3;
Section 3 Market surveillance Article 88 Market surveillance activities 1. The competent authorities shall perform appropriate checks on the conformity characteristics and performance of devices including, where appropriate, a review of documentation and physical or laboratory checks, on the basis of adequate samples. The competent authorities shall, in particular, take account of established principles regarding risk assessment and risk management, vigilance data and complaints.		SECTION 3 Market surveillance Article 93 Market surveillance activities 1. The competent authorities shall perform appropriate checks on the conformity characteristics and performance of devices including, where appropriate, a review of documentation and physical or laboratory checks, on the basis of adequate samples. The competent authorities shall, in particular, take account of established principles regarding risk assessment and risk management, vigilance data and complaints.		Market surveillance Market surveillance activities 130. —(1) The Secretary of State must— (b) take account of established principles regarding risk assessment and risk management, vigilance data and complaints.

ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS *In Vitro Diagnostic Devices.*		ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS *Medical Devices*		SCHEDULE 3 Regulation 1A General safety and performance requirements for general medical Devices
CHAPTER I GENERAL REQUIREMENTS		CHAPTER I GENERAL REQUIREMENTS		PART 1 General requirements
1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose.		1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose.		1. Devices must— (a) achieve the performance intended by their manufacturer; (b) be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose;

They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. 2. The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio. 3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall: (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability; and (f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.		They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. 2. The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio. 3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall: (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; and (f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.		(c) be safe and effective and not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. 2. The requirement in this Schedule to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio. 3.—(1) Manufacturers must establish, implement, document and maintain a risk management system. (2) Risk management is to be understood as a continuous iterative process throughout the entire lifecycle of a device, which requires regular systematic updating and, in carrying out risk management, manufacturers must— (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in sub-paragraph (c) in accordance with the requirements of paragraph 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; (f) based on the evaluation of the impact of the information referred to in paragraph 4 (e), if necessary amend control measures in line with the requirements of paragraph 4.

4. Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, the manufacturer shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority: (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety. (warnings/precautions/contra-indications) and, where appropriate, training to users. Manufacturers shall inform users of any residual risks. 5. In eliminating or reducing risks related to use error, the manufacturer shall: (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users). 6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.		4. Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, Manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority: (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users. Manufacturers shall inform users of any residual risks. 5. In eliminating or reducing risks related to use error, the manufacturer shall: (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users). 6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.		4.—(1) Risk control measures adopted by manufacturers for the design and manufacture of the devices must conform to safety principles, taking account of the generally acknowledged state of the art. (2) To reduce risks, manufacturers must manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. (3) In selecting the most appropriate solutions, manufacturers must, in the following order of priority— (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety (warnings, precautions, contra-indications) and, where appropriate, training to users; (d) inform users of any residual risks. 5. In eliminating or reducing risks related to use error, the manufacturer must— (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety); (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users). 6. The characteristics and performance of a device must not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.

7. Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer. 8. All known and foreseeable risks, and any undesirable effects shall be minimised and be acceptable when weighed against the evaluated potential benefits to the patients and/or the user arising from the intended performance of the device during normal conditions of use		7. Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer. 8. All known and foreseeable risks, and any undesirable side-effects, shall be minimised and be acceptable when weighed against the evaluated benefits to the patient and/or user arising from the achieved performance of the device during normal conditions of use. 9. For the devices referred to in Annex XVI, the general safety requirements set out in Sections 1 and 8 shall be understood to mean that the device, when used under the conditions and for the purposes intended, does not present a risk at all or presents a risk that is no more than the maximum acceptable risk related to the product's use which is consistent with a high level of protection for the safety and health of persons.		7. Devices must be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer. 8. All known and foreseeable risks, and any undesirable side-effects, must be minimized and be acceptable when weighed against the evaluated benefits to the patient or user arising from the achieved performance of the device during normal conditions of use. 9. For the devices referred to in Schedule 16, the general safety requirements set out in paragraphs 1 and 8 must be understood to mean that the device, when used under the conditions and for the purposes intended, does not present a risk at all or presents a risk that is no more than the maximum acceptable risk related to the product's use which is consistent with a high level of protection for the safety and health of persons.

ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS In Vitro Diagnostic Devices.		ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS Medical Devices		SCHEDULE 3 Regulation 1A General safety and performance requirements for general medical Devices
CHAPTER II REQUIREMENTS REGARDING PERFORMANCE, DESIGN AND MANUFACTURE		CHAPTER II REQUIREMENTS REGARDING DESIGN AND MANUFACTURE		PART 2 Requirements regarding design and manufacture
16. Electronic programmable systems—devices that incorporate electronic programmable systems and software that are devices in themselves 16 2. For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.		17. Electronic programmable systems—devices that incorporate electronic programmable systems and software that are devices in themselves 17 2. For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.		Electronic programmable systems—devices that incorporate electronic programmable systems and software that are devices in themselves 17. (2) For devices that incorporate software or for software that are devices in themselves, the software must be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.

There are requirements for single use devices in the IVDR but none comparable to the requirements of either MRD and UK requirements quoted here.		23.4. Information in the instructions for use The instructions for use shall contain all of the following particulars: (p) if the device bears an indication that it is for single use, information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used. This information shall be based on a specific section of the manufacturer's risk management documentation, where such characteristics and technical factors shall be addressed in detail. If in accordance with point (d) of Section 23.1. no instructions for use are required, this information shall be made available to the user upon request;		PART 3 Requirements regarding instructions for use Label and instructions for use Information in instructions for use 23. (6) The instructions for use must contain all the following particulars— (p) if the device bears an indication that it is for single use— (i) information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used; (ii) the information must be based on a specific section of the manufacturer's risk management documentation, where such characteristics and technical factors must be addressed in detail; (iii) if, in accordance with sub-paragraph (3)(d), no instructions for use are required, this information must be made available to the user upon request;

ANNEX II TECHNICAL DOCUMENTATION		ANNEX II TECHNICAL DOCUMENTATION		SCHEDULE 4 Regulation 1A Device description and specification including variants and accessories Technical Documentation
5. BENEFIT-RISK ANALYSIS AND RISK MANAGEMENT The documentation shall contain information on: (a) the benefit-risk analysis referred to in Sections 1 and 8 of Annex I, and (b) the solutions adopted and the results of the risk management referred to in Section 3 of Annex I.		5. BENEFIT-RISK ANALYSIS AND RISK MANAGEMENT The documentation shall contain information on: (a) the benefit-risk analysis referred to in Sections 1 and 8 of Annex I, and (b) the solutions adopted and the results of the risk management referred to in Section 3 of Annex I.		Benefit-risk analysis and risk management 6. The technical documentation must contain information on— (a) the benefit-risk analysis referred to in paragraphs 1 and 8 of Schedule 3; (b) the solutions adopted and the results of the risk management referred to in paragraph 3 of Schedule 3.

ANNEX III TECHNICAL DOCUMENTATION ON POST-MARKET SURVEIL-LANCE (b) The post-market surveillance plan shall cover at least: —suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I;		ANNEX III TECHNICAL DOCUMENTATION ON POST-MARKET SURVEILLANCE (b) The post-market surveillance plan shall cover at least: —suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I;		SCHEDULE 5 Regulation 1A Technical documentation on post-market surveillance 1. (3) The post-market surveillance plan must— (b) cover at least— (iii) suitable indicators and threshold values that must be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in paragraph 3 of Schedule 3;

These requirements given in EU MD and MDR do not seem to be in the UK Legislation.

ANNEX VII REQUIREMENTS TO BE MET BY NOTIFIED BODIES 3. RESOURCE REQUIREMENTS 3.2. Qualification criteria in relation to personnel 3.2.5. . ... — appropriate knowledge and experience of risk management and related device standards and guidance documents; 3.2.6. . ... — appropriate knowledge and experience of risk management and related device standards and guidance documents; 4. PROCESS REQUIREMENTS 4.5. Conformity assessment activities 4.5.1. General . . . . — address the interface between the manufacturer's risk management process and its appraisal and analysis of the pre-clinical and clinical evaluation and to evaluate their relevance for the demonstration of conformity with the relevant requirements in Annex I, 4.5.3. Product verification Assessment of the technical documentation — the allocation of appropriately qualified and authorised personnel for the examination of individual aspects such as use of the device, biocompatibility, clinical evaluation, risk management, and sterilisation, and . .. 4.5.4. Performance evaluation assessment. . ... (c) the interface with the risk management process, ... The notified body shall ensure that the performance evaluation adequately addresses the relevant safety and performance requirements provided for in Annex I, that it is appropriately aligned with the risk management requirements and that it is conducted in accordance with Annex XIII and that it is appropriately reflected in the information provided relating to the device.		ANNEX VII REQUIREMENTS TO BE MET BY NOTIFIED BODIES 3. RESOURCE REQUIREMENTS 3.2. Qualification criteria in relation to personnel 3.2.5. . ... — appropriate knowledge and experience of risk management and related device standards and guidance documents; 3.2.6. . ... — appropriate knowledge and experience of risk management and related device standards and guidance documents; 4. PROCESS REQUIREMENTS 4.5. Conformity assessment activities 4.5.1. General . . . . — address the interface between the manufacturer's risk management process and its appraisal and analysis of the pre-clinical and clinical evaluation and to evaluate their relevance for the demonstration of conformity with the relevant requirements in Annex I, 4.5.3. Product verification Assessment of the technical documentation — the allocation of appropriately qualified and authorised personnel for the examination of individual aspects such as use of the device, biocompatibility, clinical evaluation, risk management, and sterilisation, and . .. 4.5.4. Pre-clinical evaluation assessment. . ... (c) the interface with the risk management process, and. . . . . . 4.5.5. Clinical evaluation assessment. . . . . — the interface with the risk management process, ...The notified body shall ensure that the clinical evaluation adequately addresses the relevant safety and performance requirements provided for in Annex I, that it is appropriately aligned with the risk management requirements, that it is conducted in accordance with Annex XIV and that it is appropriately reflected in the information provided relating to the device.		

4.8. Decisions and certifications — decide, based on the results of its assessment of the performance evaluation and risk management whether the post-market surveillance plan, including the PMPF plan, is adequate, 4.11. Re-certification . . .. (c) experience from risk-management		4.8. Decisions and Certifications . .. — decide, based on the results of its assessment of the clinical evaluation and risk management, whether the post-market surveillance plan, including the PMCF plan, is adequate, 4.11. Re-certification . . ... (c) experience from risk management,		

ANNEX IX CONFORMITY ASSESSMENT BASED ON A QUALITY MANAGEMENT SYSTEM AND ON ASSESSMENT OF TECHNICAL DOCUMENTATION CHAPTER I QUALITY MANAGEMENT SYSTEM 2. Quality management system assessment 2.2. ...Moreover, the documentation to be submitted for the assessment of the quality management system shall include an adequate description of, in particular: (c) the procedures and techniques for monitoring, verifying, validating and controlling the design of the devices, and the corresponding documentation as well as the data and records arising from those procedures and techniques. Those procedures and techniques shall specifically cover: — risk management as referred to in Section 3 of Annex I, 3. Surveillance assessment 3.2. The manufacturer shall give authorisation to the notified body to carry out all the necessary audits, including on-site audits, and supply it with all relevant information, in particular: — the data stipulated in the part of the quality management system relating to design, such as the results of analyses, calculations, tests and the solutions adopted regarding the risk-management as referred to in Section 4 of Annex I,		ANNEX IX CONFORMITY ASSESSMENT BASED ON A QUALITY MANAGEMENT SYSTEM AND ON ASSESSMENT OF TECHNICAL DOCUMENTATION CHAPTER I QUALITY MANAGEMENT SYSTEM 2. Quality management system assessment 2.3. ...Moreover, the documentation to be submitted for the assessment of the quality management system shall include an adequate description of, in particular: (c) the procedures and techniques for monitoring, verifying, validating and controlling the design of the devices and the corresponding documentation as well as the data and records arising from those procedures and techniques. Those procedures and techniques shall specifically cover: — risk management as referred to in Section 3 of Annex I, 3. Surveillance assessment 3.2. The manufacturer shall give authorisation to the notified body to carry out all the necessary audits, including on-site audits, and supply it with all relevant information, in particular: — the data stipulated in the part of the quality management system relating to design, such as the results of analyses, calculations, tests and the solutions adopted regarding the risk-management as referred to in Section 4 of Annex I, and		SCHEDULE 10 Regulation 1A Conformity assessment based on quality management system on assessment of technical documentation Chapter 1 Quality management system Quality management system assessment (4) The documentation to be submitted for the assessment of the quality management system must include an adequate description of, in particular— d) those procedures and techniques must specifically cover— (ii) risk management as refered to in paragraph 3 of Schedule 3; Surveillance (7) The manufacturer must— (b) supply the notified body with all relevant information, in particular— (iii) the data stipulated in the part of the quality management system relating to design, such as the results of analyses, calculations, tests and the solutions adopted regarding the risk-management as referred to in paragraph 4 of Schedule 3;
				SCHEDULE 13 Regulation 1A Procedure for custom-made devices For information this must include all the requirements of Schedule 3 details of any areas not fully met.

ANNEX IX CONFORMITY ASSESSMENT BASED ON A QUALITY MANAGEMENT SYSTEM AND ON ASSESSMENT OF TECHNICAL DOCUMENTATION		ANNEX IX CONFORMITY ASSESSMENT BASED ON A QUALITY MANAGEMENT SYSTEM AND ON ASSESSMENT OF TECHNICAL DOCUMENTATION		SCHEDULE 10 Regulation 14A Conformity assessment based on quality management system on assessment of technical documentation
CHAPTER II ASSESSMENT OF THE TECHNICAL DOCUMENTATION 4. Assessment of the technical documentation of class B, C and D devices and batch verification applicable to class D devices 4.6. The notified body shall verify that the clinical evidence and the performance evaluation are adequate and shall verify the conclusions drawn by the manufacturer on the conformity with the relevant general safety and performance requirements. That verification shall include consideration of the adequacy of the benefit-risk determination, the risk management, the instructions for use, the user training and the manufacturer's post-market surveillance plan, and include a review of the need for, and the adequacy of, the PMPF plan proposed, where applicable.		CHAPTER II ASSESSMENT OF THE TECHNICAL DOCUMENTATION 4. Assessment of the technical documentation applicable to class III devices and to the class IIb devices referred to in the second subparagraph of Article 52(4) 4.6. The notified body shall verify that the clinical evidence and the clinical evaluation are adequate and shall verify the conclusions drawn by the manufacturer on the conformity with the relevant general safety and performance requirements. That verification shall include consideration of the adequacy of the benefit-risk determination, the risk management, the instructions for use, the user training and the manufacturer's post-market surveillance plan, and include a review of the need for, and the adequacy of, the PMCF plan proposed, where applicable.		

IVDR ANNEX XIII PERFORMANCE EVALUATION, PERFORMANCE STUDIES AND POST-MARKET PERFORMANCE FOLLOW-UP is equivalent to ANNEX XIV CLINICAL EVALUATION AND POST-MARKET CLINICAL FOLLOW-UP in the fact that they require similar risk management and device vigilance but from two different types of devices.

ANNEX XIII PERFORMANCE EVALUATION, PERFORMANCE STUDIES AND POST-MARKET PERFORMANCE FOLLOW-UP		ANNEX XIV CLINICAL EVALUATION AND POST-MARKET CLINICAL FOLLOW-UP		SCHEDULE 14 Regulation 1A Clinical evaluation and post market clinical follow-up
All below is given as it is referenced in Part B 5, 5.2, (d) below. PART A PERFORMANCE EVALUATION AND PERFORMANCE STUDIES 1 3. 1. PERFORMANCE EVALUATION 1.3. Clinical evidence and performance evaluation report 1.3.1. The manufacturer shall assess all relevant scientific validity, analytical and clinical performance data to verify the conformity of its device with the general safety and performance requirements as referred to in Annex I. The amount and quality of that data shall allow the manufacturer to make a qualified assessment whether the device will achieve the intended clinical benefit or benefits and safety, when used as intended by the manufacturer. The data and conclusions drawn from this assessment shall constitute the clinical evidence for the device. The clinical evidence shall scientifically demonstrate that the intended clinical benefit or benefits and safety will be achieved according to the state of the art in medicine. 1.3.2. Performance evaluation report The clinical evidence shall be documented in a performance evaluation report. This report shall include the scientific validity report, the analytical performance report, the clinical performance report and an assessment of those reports allowing demonstration of the clinical evidence. The performance evaluation report shall in particular include: — the justification for the approach taken to gather the clinical evidence; — the literature search methodology and the literature search protocol and literature search report of a literature review; — the technology on which the device is based, the intended purpose of the device and any claims made about the device's performance or safety; — the nature and extent of the scientific validity and the analytical and clinical performance data that has been evaluated; — the clinical evidence as the acceptable performances against the state of the art in medicine; — any new conclusions derived from PMPF reports in accordance with Part B of this Annex. 1.3.3. The clinical evidence and its assessment in the performance evaluation report shall be updated throughout the life cycle of the device concerned with data obtained from the implementation of the manufacturer's PMPF plan in accordance with Part B of this Annex, as part of the performance evaluation and the post-market surveillance system referred to in Article 10(9). The performance evaluation report shall be part of the technical documentation. Both favourable and unfavourable data considered in the performance evaluation shall be included in the technical documentation.		The following part shown for reference as it is referenced in Part B 6, 6.2 (d) below** PART A CLINICAL EVALUATION 4. The results of the clinical evaluation and the clinical evidence on which it is based shall be documented in a clinical evaluation report which shall support the assessment of the conformity of the device. The clinical evidence together with non-clinical data generated from non-clinical testing methods and other relevant documentation shall allow the manufacturer to demonstrate conformity with the general safety and performance requirements and shall be part of the technical documentation for the device in question. Both favourable and unfavourable data considered in the clinical evaluation shall be included in the technical documentation.		The following part shown for reference as it is referenced in Part B 5 (3) (d) below** Part A Clinical evaluation 3. (4) The results of the clinical evaluation and the clinical evidence on which it is based must be documented in a clinical evaluation report which— (a) must support the assessment of the conformity of the device; (b) must include any non-clinical data generated from non-clinical testing and other relevant documentation which must allow the manufacturer to demonstrate conformity with the general safety and performance requirements and which must be part of the technical documentation for the device in question; (c) must include as part of the technical documentation favourable and unfavourable data considered in the clinical evaluation.
PART B		PART B		PART B

POST-MARKET PERFORMANCE FOLLOW-UP		POST-MARKET CLINICAL FOLLOW-UP		Post-market clinical follow-up (PMCF)
5. PMPF shall be performed pursuant to a documented method laid down in a PMPF plan. 5.2. The PMPF plan shall include at least: (d) a reference to the relevant parts of the performance evaluation report referred to in Section 1.3 of this Annex and to the risk management referred to in Section 3 of Annex I; 7. The conclusions of the PMPF evaluation report shall be taken into account for the performance evaluation referred to in Article 56 and Part A of this Annex and in the risk management referred to in Section 3 of Annex I. If, through the PMPF, the need for preventive and/or corrective measures has been identified, the manufacturer shall implement them.		6. PMCF shall be performed pursuant to a documented method laid down in a PMCF plan. 6.2. The PMCF plan shall include at least: (d) a reference to the relevant parts of the clinical evaluation report referred to in Section 4 and to the risk management referred to in Section 3 of Annex I; 8. The conclusions of the PMCF evaluation report shall be taken into account for the clinical evaluation referred to in Article 61 and Part A of this Annex and in the risk management referred to in Section 3 of Annex I. If, through the PMCF, the need for preventive and/or corrective measures has been identified, the manufacturer shall implement them.		5.—(1) PMCF must be performed pursuant to a documented method laid down in a PMCF plan. (3) The PMCF plan must include at least— (d) a reference to the relevant parts of the clinical evaluation report referred to in paragraph 3(4)*** and to the risk management referred to in paragraph 3 of Schedule 3; 7. (1) The conclusions of the PMCF evaluation report must be taken into account— (i) for the clinical evaluation referred to in regulation 10(2) and Part A of this Schedule; (ii) in the risk management referred to in paragraph 3 of Schedule 3; (2) If, through the PMCF, the need for preventive or corrective measures has been identified, the manufacturer must implement them.

		ANNEX XV CLINICAL INVESTIGATIONS		SCHEDULE 15 Regulation 1A Clinical investigations
		CHAPTER II DOCUMENTATION REGARDING THE APPLICATION FOR CLINICAL INVESTIGATION 2. Investigator's Brochure *(IB)* The investigator's brochure (IB) shall contain the clinical and non-clinical information on the investigational device that is relevant for the investigation and available at the time of application. Any updates to the IB or other relevant information that is newly available shall be brought to the attention of the investigators in a timely manner. The IB shall be clearly identified and contain in particular the following information: 2.5. Summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks, any undesirable side-effects, contraindications and warnings. 2.6. In the case of devices that incorporate a medicinal substance, including a human blood or plasma derivative or devices manufactured utilising non-viable tissues or cells of human or animal origin, or their derivatives, detailed information on the medicinal substance or on the tissues, cells or their derivatives, and on the compliance with the relevant general safety and performance requirements and the specific risk management in relation to the substance or tissues, cells or their derivatives, as well as evidence for the added value of incorporation of such constituents in relation to the clinical benefit and/or safety of the device.		Chapter II Documentation regarding the application for clinical investigation Investigator's brochure *(IB)* 2. (1) An investigator's brochure (IB) must contain the clinical and non-clinical information on the investigational device that is relevant for the investigation and available at the time of application. (2) Any updates to the IB or other relevant information that is newly available must be brought to the attention of the investigators in a timely manner. (3) The IB must be clearly identified and contain in particular the following information— (e) a summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks, any undesirable effects, contraindications and warnings; (f) in the case of devices that incorporate a medicinal substance, including a human blood or plasma derivative or devices manufactured utilising non-viable tissues or cells of human or animal origin, or their derivatives, detailed information on the medicinal substance or on the tissues, cells or their derivatives, and on the compliance with the relevant general safety and performance requirements and the specific risk management in relation to the substance or tissues, cells or their derivatives, as well as evidence for the added value of incorporation of such constituents in relation to the clinical benefit or safety of the device;

		ANNEX XIV CLINICAL EVALUATION AND POST-MARKET CLINICAL FOLLOW-UP		SCHEDULE 14 Regulation 1A Clinical evaluation and post-market clinical follow-up
		The following part shown for reference as it is referenced in Part B 6, 6.2 (d) below** PART A CLINICAL EVALUATION 4. The results of the clinical evaluation and the clinical evidence on which it is based shall be documented in a clinical evaluation report which shall support the assessment of the conformity of the device. The clinical evidence together with non-clinical data generated from non-clinical testing methods and other relevant documentation shall allow the manufacturer to demonstrate conformity with the general safety and performance requirements and shall be part of the technical documentation for the device in question. Both favourable and unfavourable data considered in the clinical evaluation shall be included in the technical documentation.		The following part shown for reference as it is referenced in Part B 5 (3) (d) below** Part A Clinical evaluation 3. (4) The results of the clinical evaluation and the clinical evidence on which it is based must be documented in a clinical evaluation report which— (a) must support the assessment of the conformity of the device; (b) must include any non-clinical data generated from non-clinical testing and other relevant documentation which must allow the manufacturer to demonstrate conformity with the general safety and performance requirements and which must be part of the technical documentation for the device in question; (c) must include as part of the technical documentation favourable and unfavourable data considered in the clinical evaluation.
		PART B POST-MARKET CLINICAL FOLLOW-UP		PART B Post–market clinical follow-up (PMCF)
		6. PMCF shall be performed pursuant to a documented method laid down in a PMCF plan. 6.2. The PMCF plan shall include at least: (d) a reference to the relevant parts of the clinical evaluation report referred to in Section 4 and to the risk management referred to in Section 3 of Annex I; 8. The conclusions of the PMCF evaluation report shall be taken into account for the clinical evaluation referred to in Article 61 and Part A of this Annex and in the risk management referred to in Section 3 of Annex I. If, through the PMCF, the need for preventive and/or corrective measures has been identified, the manufacturer shall implement them.		5.—(1) PMCF must be performed pursuant to a documented method laid down in a PMCF plan. (3) The PMCF plan must include at least— (d) a reference to the relevant parts of the clinical evaluation report referred to in paragraph 3(4)** and to the risk management referred to in paragraph 3 of Schedule 3; 7. (1) The conclusions of the PMCF evaluation report must be taken into account— (i) for the clinical evaluation referred to in regulation 10(2) and Part A of this Schedule; (ii) in the risk management referred to in paragraph 3 of Schedule 3; (2) If, through the PMCF, the need for preventive or corrective measures has been identified, the manufacturer must implement them.

		ANNEX XV CLINICAL INVESTIGATIONS		SCHEDULE 15 Regulation 1A Clinical investigations
		CHAPTER II DOCUMENTATION REGARDING THE APPLICATION FOR CLINICAL INVESTIGATION 2. Investigator's Brochure *(IB)* The investigator's brochure (IB) shall contain the clinical and non-clinical information on the investigational device that is relevant for the investigation and available at the time of application. Any updates to the IB or other relevant information that is newly available shall be brought to the attention of the investigators in a timely manner. The IB shall be clearly identified and contain in particular the following information: 2.5. Summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks, any undesirable side-effects, contraindications and warnings. 2.6. In the case of devices that incorporate a medicinal substance, including a human blood or plasma derivative or devices manufactured utilising non-viable tissues or cells of human or animal origin, or their derivatives, detailed information on the medicinal substance or on the tissues, cells or their derivatives, and on the compliance with the relevant general safety and performance requirements and the specific risk management in relation to the substance or tissues, cells or their derivatives, as well as evidence for the added value of incorporation of such constituents in relation to the clinical benefit and/or safety of the device.		Chapter II Documentation regarding the application for clinical investigation Investigator's brochure *(IB)* 2. (1) An investigator's brochure (IB) must contain the clinical and non-clinical information on the investigational device that is relevant for the investigation and available at the time of application. (2) Any updates to the IB or other relevant information that is newly available must be brought to the attention of the investigators in a timely manner. (3) The IB must be clearly identified and contain in particular the following information— (e) a summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks, any undesirable effects, contraindications and warnings; (f) in the case of devices that incorporate a medicinal substance, including a human blood or plasma derivative or devices manufactured utilising non-viable tissues or cells of human or animal origin, or their derivatives, detailed information on the medicinal substance or on the tissues, cells or their derivatives, and on the compliance with the relevant general safety and performance requirements and the specific risk management in relation to the substance or tissues, cells or their derivatives, as well as evidence for the added value of incorporation of such constituents in relation to the clinical benefit or safety of the device;

Review of MDR only to relevant UK requirements.

CHAPTER I INTRODUCTORY PROVISIONS CHAPTER II MAKING AVAILABLE ON THE MARKET AND PUTTING INTO SERVICE OF DEVICES, OBLIGATIONS OF ECONOMIC OPERATORS, CE MARKING, FREE MOVEMENT				"PART IX The rights, powers, liabilities, obligations, restrictions, remedies and procedures recognised under the in vitro diagnostic Medical Devices Regulation (see regulation 4P) Scope and definitions
Article 8 Use of harmonised standards 1. Devices that are in conformity with the relevant harmonised standards, or the relevant parts of those standards, the references of which have been published in the Official Journal of the European Union, shall be presumed to be in conformity with the requirements of this Regulation covered by those standards or parts thereof. The first subparagraph shall also apply to system or process requirements to be fulfilled in accordance with this Regulation by economic operators or sponsors, including those relating to quality management systems, risk management, post-market surveillance systems, performance studies, clinical evidence or post-market performance follow-up ("PMPF"). Article 10 General obligations of manufacturers 2. Manufacturers shall establish, document, implement and maintain a system for risk management as described in Section 3 of Annex I. 8 . . . . The quality management system shall address at least the following aspects: (e) risk management as set out in Section 3 of Annex I;				Use of standards 143.—(1) Devices that are in conformity with the designated standards, or the relevant parts of those standards, are presumed to be in conformity with the requirements of this Part which cover those designated standards or relevant parts of those standards. (2) Paragraph (1) also applies to system or process requirements to be fulfilled in accordance with this Part by economic operators or sponsors, including those relating to quality management systems, risk management, post-market surveillance systems, performance studies, clinical evaluation or post-market performance follow-up ("PMPF"). General obligations of manufacturers 145. (2) Manufacturers must establish, document, implement and maintain a system for risk management as described in paragraph 3 of Schedule 17. (13) The quality management system required by paragraph (12) must—. . . . . (v) risk management as set out in paragraph 3 of Schedule 17;

CHAPTER VII POST-MARKET SURVEILLANCE, VIGILANCE AND MARKET SURVEILLANCE Section 1 Post–market surveillance Article 78 Post-market surveillance system of the manufacturer 3. Data gathered by the manufacturer's post-market surveillance system shall in particular be used: (a) to update the benefit-risk determination and to improve the risk management as referred to in Chapter I of Annex I;				Post-market surveillance, vigilance and market surveillance Post-market surveillance system of the manufacturer 186. (3) The manufacturer must ensure that— (a) data gathered by the manufacturer's post-market surveillance system is used in particular— (i) to update the benefit-risk determination and to improve the risk management as referred to in Part 1 of Schedule 17
Section 3 Market surveillance Article 88 Market surveillance activities 1. The competent authorities shall perform appropriate checks on the conformity characteristics and performance of devices including, where appropriate, a review of documentation and physical or laboratory checks on the basis of adequate samples. The competent authorities shall, in particular, take account of established principles regarding risk assessment and risk management, vigilance data and complaints.				Market surveillance Market surveillance activities 195. (1) The Secretary of State must— (a) perform appropriate checks on the conformity characteristics and performance of devices including, where appropriate, a review of documentation and physical or laboratory checks on the basis of adequate samples; (b) in doing so, take account of established principles regarding risk assessment and risk management, vigilance data and complaints.

ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS *In Vitro Diagnostic Devices*:		N/A		SCHEDULE 7 / Regulation 7A General safety and performance requirements - in vitro diagnostic medical devices
CHAPTER I GENERAL REQUIREMENTS		N/A		PART 1 General requirements for in vitro diagnostic medical devices
1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. 2. The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio. 3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall: (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability; and (f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.		N/A		1. Devices must— (a) achieve the performance intended by their manufacturer; (b) be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose; (c) be safe and effective; (d) not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks, which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art. 2. The requirement in this Schedule to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio. 3.—(1) Manufacturers must establish, implement, document and maintain a risk management system. (2) Risk management must be understood as a continuous, iterative process throughout the entire lifecycle of a device, requiring regular systematic updating and in carrying out risk management manufacturers must— (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in sub-paragraph (c) in accordance with the requirements of paragraph 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability; (f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of paragraph 4.	

4. Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, the manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority: (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety. (warnings/precautions/contra-indications) and, where appropriate, training to users. Manufacturers shall inform users of any residual risks. 5. In eliminating or reducing risks related to use error, the manufacturer shall: (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users). 6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions. 7. Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer. 8. All known and foreseeable risks, and any undesirable effects shall be minimised and be acceptable when weighed against the evaluated potential benefits to the patients and/or the user arising from the intended performance of the device during normal conditions of use.		N/A		4.—(1) Risk control measures adopted by manufacturers for the design and manufacture of the devices must conform to safety principles, taking account of the generally acknowledged state of the art. (2) To reduce risks, the manufacturers must manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. (3) In selecting the most appropriate solutions, manufacturers must, in the following order of priority— (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; (c) provide information for safety (warnings, precautions, contra-indications) and, where appropriate, training to users; (d) inform users of any residual risks. 5. In eliminating or reducing risks related to use error, the manufacturer must— (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety); (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users). 6. The characteristics and performance of a device must not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions. 7. Devices must be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer. 8. All known and foreseeable risks, and any undesirable effects must be minimised and be acceptable when weighed against the evaluated potential benefits to the patients or the user arising from the intended performance of the device during normal conditions of use.		

CHAPTER II REQUIREMENTS REGARDING PERFORMANCE, DESIGN AND MANUFACTURE		N/A		PART 2 Requirements regarding design and manufacture of in vitro diagnostic medical devices
16. Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves 16.2. For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.		N/A		Electronic programmable systems- devices that incorporate programmable systems and software that are devices in themselves 16. (2) For devices that incorporate software or for software that is a device in itself , the software must be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.
ANNEX II TECHNICAL DOCUMENTATION		N/A		SCHEDULE 18 Regulation 1A Technical documentation - in vitro diagnostic medical devices
5. BENEFIT-RISK ANALYSIS AND RISK MANAGEMENT The documentation shall contain information on: (a) the benefit-risk analysis referred to in Sections 1 and 8 of Annex I, and (b) the solutions adopted and the results of the risk management referred to in Section 3 of Annex I.		N/A		Benefit-risk analysis and risk management 6. The documentation must contain information on— (a) the benefit-risk analysis referred to in paragraphs 1 and 8 of Schedule 17, (b) the solutions adopted and the results of the risk management referred to in paragraph 3 of Schedule 17.
ANNEX III TECHNICAL DOCUMENTATION ON POST-MARKET SURVEILLANCE		N/A		SCHEDULE 19 Regulation 1A Technical documentation on post-market surveillance for in vitro diagnostic medical devices
(b) The post-market surveillance plan shall cover at least: — suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I;		N/A		4. The post-market surveillance plan must cover at least— (c) suitable indicators and threshold values that must be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in paragraph 3 of Schedule 3;

ANNEX IX CONFORMITY ASSESSMENT BASED ON A QUALITY MANAGEMENT SYSTEM AND ON ASSESSMENT OF TECHNICAL DOCUMENTATION CHAPTER I QUALITY MANAGEMENT SYSTEM 2. Quality management system assessment . . . Moreover, the documentation to be submitted for the assessment of the quality management system shall include an adequate description of, in particular: (c) the procedures and techniques for monitoring, verifying, validating and controlling the design of the devices, and the corresponding documentation as well as the data and records arising from those procedures and techniques. Those procedures and techniques shall specifically cover: —risk management as referred to in Section 3 of Annex I,		N/A		SCHEDULE 4 Regulation 1A Conformity assessment based on quality management system and on assessment of technical documentation- in vitro diagnostic medical devices PART 1 Quality management system Quality management system assessment (4) The documentation to be submitted for the assessment of the quality management system must include an adequate description of, in particular— (c) the procedures and techniques for monitoring, verifying, validating and controlling the design of the devices, and the corresponding documentation as well as the data and records arising from those procedures and techniques and those procedures and techniques must specifically cover— (iii) risk management as referred to in paragraph 3 of Schedule 17;
3. Surveillance assessment 3.2. The manufacturer shall give authorisation to the notified body to carry out all the necessary audits, including on-site audits, and supply it with all relevant information, in particular: . . . —the data stipulated in the part of the quality management system relating to design, such as the results of analyses, calculations, tests and the solutions adopted regarding the risk-management as referred to in Section 4 of Annex I,		N/A		Surveillance applicable to Class C and Class D devices (7) The manufacturer of Class C and D devices must give authorisation to the notified body to carry out all the necessary audits, including on-site audits, and supply it with all relevant information, in particular— (c) the data stipulated in the part of the quality management system relating to design, such as the results of analyses, calculations, tests and the solutions adopted regarding the risk-management as referred to in paragraph 4 of Schedule 17;
CHAPTER II ASSESSMENT OF THE TECHNICAL DOCUMENTATION 4. Assessment of the technical documentation of class B, C and D devices and batch verification applicable to class D devices 4.6. The notified body shall verify that the clinical evidence and the performance evaluation are adequate and shall verify the conclusions drawn by the manufacturer on the conformity with the relevant general safety and performance requirements. That verification shall include consideration of the adequacy of the benefit-risk determination, the risk management, the instructions for use, the user training and the manufacturer's post-market surveillance plan, and include a review of the need for, and the adequacy of, the PMPF plan proposed, where applicable.		N/A		PART 2 Assessment of technical documentation Assessment of the technical documentation of class B, C and D devices and batch verification applicable to class D devices

ANNEX XIII PERFORMANCE EVALUATION, PERFORMANCE STUDIES AND POST-MARKET PERFORMANCE FOLLOW-UP		N/A		SCHEDULE 2 / Regulation 1A Performance evaluation, performance studies and post-market performance follow-up
All below is given as it is referenced in Part B 5, 5.2, (d) below. PART A PERFORMANCE EVALUATION AND PERFORMANCE STUDIES 1 3. 1. PERFORMANCE EVALUATION 1.3. Clinical evidence and performance evaluation report 1.3.1. The manufacturer shall assess all relevant scientific validity, analytical and clinical performance data to verify the conformity of its device with the general safety and performance requirements as referred to in Annex I. The amount and quality of that data shall allow the manufacturer to make a qualified assessment whether the device will achieve the intended clinical benefit or benefits and safety, when used as intended by the manufacturer. The data and conclusions drawn from this assessment shall constitute the clinical evidence for the device. The clinical evidence shall scientifically demonstrate that the intended clinical benefit or benefits and safety will be achieved according to the state of the art in medicine. 1.3.2. Performance evaluation report The clinical evidence shall be documented in a performance evaluation report. This report shall include the scientific validity report, the analytical performance report, the clinical performance report and an assessment of those reports allowing demonstration of the clinical evidence. The performance evaluation report shall in particular include: — the justification for the approach taken to gather the clinical evidence; — the literature search methodology and the literature search protocol and literature search report of a literature review; — the technology on which the device is based, the intended purpose of the device and any claims made about the device's performance or safety; — the nature and extent of the scientific validity and the analytical and clinical performance data that has been evaluated; — the clinical evidence as the acceptable performances against the state of the art in medicine; — any new conclusions derived from PMPF reports in accordance with Part B of this Annex. 1.3.3. The clinical evidence and its assessment in the performance evaluation report shall be updated throughout the life-cycle of the device concerned with data obtained from the implementation of the manufacturer's PMPF plan in accordance with Part B of this Annex, as part of the performance evaluation and the post-market surveillance system referred to in Article 10(9). The performance evaluation report shall be part of the technical documentation. Both favourable and unfavourable data considered in the performance evaluation shall be included in the technical documentation.		N/A		All below is given as it is referenced in Part B 3 (3) (d) below. PART A Performance evaluation and performance studies Performance evaluation 1. Clinical evidence and performance evaluation report (17) The manufacturer must assess all relevant scientific validity, analytical and clinical performance data to verify the conformity of its device with the general safety and performance requirements as referred to in Schedule 1 7. (18) The amount and quality of that data must allow the manufacturer to make a qualified assessment whether the device will achieve the intended clinical benefit or benefits and safety, when used as intended by the manufacturer. (19) The data and conclusions drawn from this assessment constitute the clinical evidence for the device. (20) The clinical evidence must scientifically demonstrate that the intended clinical benefit or benefits and safety will be achieved according to the state of the art in medicine.
PART B POST-MARKET PERFORMANCE FOLLOW-UP		N/A		PART B Post-market performance follow-up (PMPF)

5. PMPF shall be performed pursuant to a documented method laid down in a PMPF plan. 5.2. The PMPF plan shall include at least: (d) a reference to the relevant parts of the performance evaluation report referred to in Section 1.3 of this Annex and to the risk management referred to in Section 3 of Annex I; 7. The conclusions of the PMPF evaluation report shall be taken into account for the performance evaluation referred to in Article 56 and Part A of this Annex and in the risk management referred to in Section 3 of Annex I. If, through the PMPF, the need for preventive and/or corrective measures has been identified, the manufacturer shall implement them.				5.—(1) PMPF shall be performed pursuant to a documented method laid down in a PMPF plan. (3) The PMPF plan shall include at least— (d) reference to the relevant parts of the performance evaluation report referred to in sub-paragraphs (17) to (20) of paragraph 1 of this Schedule and to the risk management referred to in paragraph 3 of Schedule 17; 7. The conclusions of the PMPF evaluation report must be taken into account for the performance evaluation referred to in regulation 167 and Part A of this Schedule and in the risk management referred to in paragraph 3 of Schedule 17 and, if, through the PMPF, the need for preventive or corrective measures has been identified, the manufacturer must implement them.

ANNEX XIV INTERVENTIONAL CLINICAL PERFORMANCE STUDIES AND CERTAIN OTHER PERFORMANCE STUDIES		N/A		SCHEDULE 28 Regulation 1A Interventional clinical performance studies and certain other performance studies
CHAPTER I DOCUMENTATION REGARDING THE APPLICATION FOR INTERVENTIONAL CLINICAL PERFORMANCE STUDIES AND OTHER PERFORMANCE STUDIES INVOLVING RISKS FOR THE SUBJECTS OF THE STUDIES		N/A		PART I Documentation regarding the application for interventional clinical performance studies and other performance studies involving risks for the subjects of the studies
2. Investigator's brochure The investigator's brochure (IB) shall contain the information on the device for performance study that is relevant for the study and available at the time of application. Any updates to the IB or other relevant information that is newly available shall be brought to the attention of the investigators in a timely manner. The IB shall be clearly identified and contain in particular the following information: 2.5. Summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks and warnings. 2.6. In the case of devices that include tissues, cells and substances of human, animal or microbial origins detailed information on the tissues, cells and substances, and on the compliance with the relevant general safety and performance requirements and the specific risk management in relation to those tissues, cells and substances.		N/A		Investigator's brochure 2. (2) The IB *(investigator's brochure)* must be clearly identified and contain in particular the following information— (f) summary of the benefit-risk analysis and the risk management, including information regarding known or foreseeable risks and warnings; (g) in the case of devices that include tissues, cells and substances of human, animal or microbial origins detailed information on the tissues, cells and substances, and on the compliance with the relevant general safety and performance requirements and the specific risk management in relation to those tissues, cells and substances;

Appendix C4 7 Comparison: in vitro diagnostic Devices classification rules – UK v EU

ANNEX VIII CLASSIFICATION RULES		SCHEDULE 23 Regulation 1A Classification Rules for in vitro diagnostic medical devices
1. IMPLEMENTING RULES 1.1. Application of the classification rules shall be governed by the intended purpose of the devices. 1.2. If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices. 1.3. Accessories for an in vitro diagnostic medical device shall be classified in their own right separately from the device with which they are used. 1.4. Software, which drives a device or influences the use of a device, shall fall within the same class as the device. If the software is independent of any other device, it shall be classified in its own right. 1.5. Calibrators intended to be used with a device shall be classified in the same class as the device.		Implementation rules 1.—(1) Application of the classification rules must be governed by the intended purpose of the devices. (2) If the device in question is intended to be used in combination with another device, the classification rules must apply separately to each of the devices. (3) Accessories for an in vitro diagnostic medical device must be classified in their own right separately from the device with which they are used. (4) Software which— (a) drives a device or influences the use of a device, must fall within the same class as the device; (b) is independent of any other device, must be classified in its own right. (5) Calibrators intended to be used with a device must be classified in the same class as the device.

1.6. Control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes shall be classified in the same class as the device.		(6) Control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes must be classified in the same class as the device.
1.7. The manufacturer shall take into consideration all classification and implementation rules in order to establish the proper classification for the device.		(7) The manufacturer must take into consideration all classification and implementation rules in order to establish the proper classification for the device.
1.8. Where a manufacturer states multiple intended purposes for a device, and as a result the device falls into more than one class, it shall be classified in the higher class.		(8) Where a manufacturer states multiple intended purposes for a device, and as a result the device falls into more than one class, it must be classified in the higher class.
1.9. If several classification rules apply to the same device, the rule resulting in the higher classification shall apply.		(9) If several classification rules apply to the same device, the rule resulting in the higher classification must apply.
1.10. Each of the classification rules shall apply		(10) Each of the classification rules must apply to first line assays, confirmatory assays and supplemental assays.

ANNEX VIII CLASSIFICATION RULES		SCHEDULE 23 Regulation 1A Classification Rules for in vitro diagnostic medical devices
2. CLASSIFICATION RULES		Classification rules
2.1. Rule 1 Devices intended to be used for the following purposes are classified as class D: — detection of the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration; — detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation; — determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management.		Rule 1 2.—(1) Devices intended to be used for the following purposes are classified as Class D— (a) detection of the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration; (b) detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation; (c) determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management.

2.2. Rule 2 Devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as class C, except when intended to determine any of the following markers: — ABO system [A (ABO1), B (ABO2), AB (ABO3)]; — Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)]; — Kell system [Kel1 (K)]; — Kidd system [JK1 (Jka), JK2 (Jkb)]; — Duffy system [FY1 (Fya), FY2 (Fyb)]; in which case they are classified as class D.		Rule 2 (2) Devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as class C, except when intended to determine any of the following markers— (a) ABO system [A (ABO1), B (ABO2), AB (ABO3)]; (b) Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)]; (c) Kell system [Kel1 (K)]; (d) Kidd system [JK1 (Jka), JK2 (Jkb)]; (e) Duffy system [FY1 (Fya), FY2 (Fyb)]; in which case they are classified as Class D.

2.3. Rule 3 Devices are classified as class C if they are intended: (a) for detecting the presence of, or exposure to, a sexually transmitted agent; (b) for detecting the presence in cerebrospinal fluid or blood of an infectious agent without a high or suspected high risk of propagation; (c) for detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested, or to the individual's offspring; (d) for pre-natal screening of women in order to determine their immune status towards transmissible agents; (e) for determining infective disease status or immune status, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring; (f) to be used as companion diagnostics; (g) to be used for disease staging, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life- threatening situation for the patient or for the patient's offspring; (h) to be used in screening, diagnosis, or staging of cancer;		Rule 3 (3) Devices are classified as Class C if they are intended— (a) for detecting the presence of, or exposure to, a sexually transmitted agent; (b) for detecting the presence in cerebrospinal fluid or blood of an infectious agent without a high or suspected high risk of propagation; (c) for detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested, or to the individual’s offspring; (d) for pre-natal screening of women in order to determine their immune status towards transmissible agents; (e) for determining infective disease status or immune status, where there is a risk that an erroneous result would lead to a patient management decision resulting in a lifethreatening situation for the patient or for the patient’s offspring; (f) to be used as companion diagnostics; (g) to be used for disease staging, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient’s offspring; (h) to be used in screening, diagnosis, or staging of cancer;

(i) for human genetic testing; (j) for monitoring of levels of medicinal products, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring; (k) for management of patients suffering from a life-threatening disease or condition; (l) for screening for congenital disorders in the embryo or foetus; (m) for screening for congenital disorders in new-born babies where failure to detect and treat such disorder could lead to life-threatening situations or severe disabilities.		(i) for human genetic testing; (j) for monitoring of levels of medicinal products, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient’s offspring; (k) for management of patients suffering from a life-threatening disease or condition; (l) for screening for congenital disorders in the embryo or foetus; (m) for screening for congenital disorders in new-born babies where failure to detect and treat such disorders could lead to life-threatening situations or severe disabilities.

2.4. Rule 4 (a) Devices intended for self-testing are classified as class C, except for devices for the detection of pregnancy, for fertility testing and for determining cholesterol level, and devices for the detection of glucose, erythrocytes, leucocytes and bacteria in urine, which are classified as class B. (b) Devices intended for near-patient testing are classified in their own right.		Rule 4 (4) Devices intended for self-testing are classified as Class C, except for devices testing the following which are classified in Class D— (a) the detection of pregnancy; (b) fertility testing; (c) for determining cholesterol level; (d) for the detection of glucose, erythrocytes, leucocytes and bacteria in urine. (5) Devices intended for near-patient testing are classified in their own right.

2.5. Rule 5 The following devices are classified as class A: (a) products for general laboratory use, accessories which possess no critical characteristics, buffer solutions, washing solutions, and general culture media and histological stains, intended by the manufacturer to make them suitable for in vitro diagnostic procedures relating to a specific examination; (b) instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures; (c) specimen receptacles.		Rule 5 (6) The following devices are classified as Class A— (a) products for general laboratory use, accessories which possess no critical characteristics, buffer solutions, washing solutions, and general culture media and histological stains, intended by the manufacturer to make them suitable for in vitro diagnostic procedures relating to a specific examination; (b) instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures; (c) specimen receptacles.

2.6. Rule 6 Devices not covered by the above-mentioned classification rules are classified as class B.		Rule 6 Devices not covered by the above-mentioned classification rules are classified as Class B.

2.7. Rule 7 Devices which are controls without a quantitative or qualitative assigned value are classified as class B		Rule 7 Devices which are controls without a quantitative or qualitative assigned value are classified as Class B.

Appendix C4 8 Comparison: Medical Devices classification rules UK v EU

ANNEX VIII CLASSIFICATION RULES CHAPTER I DEFINITIONS SPECIFIC TO CLASSIFICATION RULES		SCHEDULE 9 Regulation 1A Classification rules Chapter 1 Definitions specific to classification rules
1. DURATION OF USE 1.1. ‘Transient’ means normally intended for continuous use for less than 60 minutes. 1.2. ‘Short term’ means normally intended for continuous use for between 60 minutes and 30 days. 1.3. ‘Long term’ means normally intended for continuous use for more than 30 days.		1. In this Schedule— (a) in relation to the duration of use— “long term” means normally intended for continuous use for more than 30 days; “short term” means normally intended for continuous use for between 60 minutes and 30 days; “transient” means normally intended for continuous use for less than 60 minutes;

2. INVASIVE AND ACTIVE DEVICES 2**.1. 'Body orifice'** means any natural opening in the body, as well as the external surface of the eyeball, or any permanent artificial opening, such as a stoma. 2.2. 'Surgically invasive device' means: (a) an invasive device which penetrates inside the body through the surface of the body, including through mucous membranes of body orifices with the aid or in the context of a surgical operation; and (b) a device which produces penetration other than through a body orifice. 2.3. '*Reusable surgical instrument'* means an instrument intended for surgical use in cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or similar procedures, without a connection to an active device and which is intended by the manufacturer to be reused after appropriate procedures such as cleaning, disinfection and sterilisation have been carried out. 2.4**. *'Active therapeutic device'*** means any active device used, whether alone or in combination with other devices, to support, modify, replace or restore biological functions or structures with a view to treatment or alleviation of an illness, injury or disability. 2.5*. 'Active device intended for diagnosis and monitoring'* means any active device used, whether alone or in combination with other devices, to supply information for detecting, diagnosing, monitoring or		(b) in relation to invasive and active devices— "*active device intended for diagnosis and monitoring*" means any active device used, whether alone or in combination with other devices, to supply information for detecting, diagnosing, monitoring or treating physiological conditions, states of health, illnesses or congenital deformities; ***"active therapeutic device"*** means any active device used, whether alone or in combination with other devices, to support, modify, replace or restore biological functions or structures with a view to treatment or alleviation of an illness, injury or disability; **"body orifice"** means any natural opening in the body, as well as the external surface of the eyeball, or any permanent artificial opening, such as a stoma; *"central circulatory system"* means the following blood vessels— arteriae pulmonales, aorta ascendens, arcus aortae, aorta descendens to the bifurcation aortae, arteriae coronariae, arteria carotis communis, arteria carotis externa, arteria carotis interna, arteriae cerebrales, truncus brachiocephalicus, venae cordis, venae pulmonales, vena cava superior and vena cava inferior; "central nervous system" means the brain, meninges and spinal cord; "injured skin or mucous membrane" means an area of skin or a mucous membrane presenting a pathological change or change following disease or a wound;

treating physiological conditions, states of health, illnesses or congenital deformities. 2.6. *'Central circulatory system'* means the following blood vessels: arteriae pulmonales, aorta ascendens, arcus aortae, aorta descendens to the bifurcatio aortae, arteriae coronariae, arteria carotis communis, arteria carotis externa, arteria carotis interna, arteriae cerebrales, truncus brachiocephalicus, venae cordis, venae pulmonales, vena cava superior and vena cava inferior. 2.7. 'Central nervous system' means the brain, meninges and spinal cord. 2.8. 'Injured skin or mucous membrane' means an area of skin or a mucous membrane presenting a pathological change or change following disease or a wound.		"*reusable surgical instrument*" means an instrument intended for surgical use in cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or similar procedures, without a connection to an active device and which is intended by the manufacturer to be reused after appropriate procedures such as cleaning, disinfection and sterilisation have been carried out; "surgically invasive device" means— (a) an invasive device which penetrates inside the body through the surface of the body, including through mucous membranes of body orifices with the aid or in the context of a surgical operation; and (b) a device which penetrates other than through a body orifice;

ANNEX VIII CLASSIFICATION RULES		SCHEDULE 9 Regulation 1A Classification rules
CHAPTER II IMPLEMENTING RULES		Chapter 2 Implementing rules
3.1. Application of the classification rules shall be governed by the intended purpose of the devices. 3.2. If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices. Accessories for a medical device shall be classified in their own right separately from the device with which they are used. 3.3. Software, which drives a device or influences the use of a device, shall fall within the same class as the device. If the software is independent of any other device, it shall be classified in its own right. 3.4. If the device is not intended to be used solely or principally in a specific part of the body, it shall be considered and classified on the basis of the most critical specified use. 3.5. If several rules, or if, within the same rule, several sub-rules, apply to the same device based on the device's intended purpose, the strictest rule and sub-rule resulting in the higher classification shall apply.		2.—(1) Application of the classification rules must be governed by the intended purpose of the devices. (2) If the device in question is intended to be used in combination with another device— (a) the classification rules must apply separately to each of the devices; (b) accessories for a medical device and for a product listed in Schedule 16 must be classified in their own right separately from the device with which they are used. (3) Software, which drives a device or influences the use of a device, must fall within the same class as the device but, if the software is independent of any other device, it must be classified in its own right. (4) If the device is not intended to be used solely or principally in a specific part of the body, it must be considered and classified on the basis of the most critical specified use. (5) If several rules or, if, within the same rule, several sub-rules, apply to the same device based on the device’s intended purpose, the strictest rule and sub-rule resulting in the higher classification must apply.

3.6. In calculating the duration referred to in Section 1, continuous use shall mean: (a) the entire duration of use of the same device without regard to temporary interruption of use during a procedure or temporary removal for purposes such as cleaning or disinfection of the device. Whether the interruption of use or the removal is temporary shall be established in relation to the duration of the use prior to and after the period when the use is interrupted or the device removed; and (b) the accumulated use of a device that is intended by the manufacturer to be replaced immediately with another of the same type. 3.7. A device is considered to allow direct diagnosis when it provides the diagnosis of the disease or condition in question by itself		(6) In calculating the duration of use referred to in paragraph 1(a), continuous use means— (a) the entire duration of use of the same device without regard to temporary interruption of use during a procedure or temporary removal for purposes such as cleaning or disinfection of the device (and, whether the interruption of use or the removal is temporary must be established in relation to the duration of the use prior to and after the period when the use is interrupted or the device removed); (b) the accumulated use of a device that is intended by the manufacturer to be replaced immediately with another of the same type. (7) A device is considered to allow direct diagnosis when it provides the diagnosis of the disease or condition in question by itself or when it provides decisive information for the diagnosis.

ANNEX VIII CLASSIFICATION RULES		SCHEDULE 9 Regulation 1A Classification rules
Chapter 3 Classification rules		Chapter 3 Classification rules
4. NON-INVASIVE DEVICES		Non-invasive devices
4.1. Rule 1 All non-invasive devices are classified as class I, unless one of the rules set out hereinafter applies.		Rule 1 3.—(1) All non-invasive devices are classified as Class I, unless one of the other rules set out in this Schedule applies.
4.2. Rule 2 All non-invasive devices intended for channelling or storing blood, body liquids, cells or tissues, liquids or gases for the purpose of eventual infusion, administration or introduction into the body are classified as class IIa: — if they may be connected to a class IIa, class IIb or class III active device; or — if they are intended for use for channelling or storing blood or other body liquids or for storing organs, parts of organs or body cells and tissues, except for blood bags; blood bags are classified as class IIb. In all other cases, such devices are classified as class I.		Rule 2 (2) All non-invasive devices intended for channelling or storing blood, body liquids, cells or tissues, liquids or gases for the purpose of eventual infusion, administration or introduction into the body are classified as Class IIa— (a) if they may be connected to a Class IIa, Class IIb or Class III active device; or (b) if they are intended for use for channelling or storing blood or other body liquids or for storing organs, parts of organs or body cells and tissues, except for blood bags which are classified as Class IIb; such devices are classified as Class I, in all other cases.

4.3. Rule 3 All non-invasive devices intended for modifying the biological or chemical composition of human tissues or cells, blood, other body liquids or other liquids intended for implantation or administration into the body are classified as class IIb, unless the treatment for which the device is used consists of filtration, centrifugation or exchanges of gas, heat, in which case they are classified as class IIa. All non-invasive devices consisting of a substance or a mixture of substances intended to be used in vitro in direct contact with human cells, tissues or organs taken from the human body or used in vitro with human embryos before their implantation or administration into the body are classified as class III		Rule 3 (3) All non-invasive devices intended for modifying the biological or chemical composition of human tissues or cells, blood, other body liquids or other liquids intended for implantation or administration into the body are classified as Class IIb, unless the treatment for which the device is used consists of filtration, centrifugation or exchanges of gas, heat, in which case they are classified as Class IIa. (4) All non-invasive devices consisting of a substance or a mixture of substances intended to be used in vitro in direct contact with human cells, tissues or organs taken from the human body or used in vitro with human embryos before their implantation or administration into the body are classified as Class III.
4.4. Rule 4 All non-invasive devices which come into contact with injured skin or mucous membrane are classified as: — class I if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates; — class IIb if they are intended to be used principally for injuries to skin which have breached the dermis or mucous membrane and can only heal by secondary intent; — class IIa if they are principally intended to manage the micro-environment of injured skin or mucous membrane; and — class IIa in all other cases.		Rule 4 (5) All non-invasive devices which come into contact with injured skin or mucous membrane are classified as— (a) Class I if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates; (b) Class IIb if they are intended to be used principally for injuries to skin which have breached the dermis or mucous membrane and can only heal by secondary intent; (c) Class IIa if they are principally intended to manage the micro-environment of injured skin or mucous membrane; (d) Class IIa in all other cases.

This rule applies also to the invasive devices that come into contact with injured mucous membrane.		This rule also applies to the invasive devices that come into contact with injured mucous membrane.

5. INVASIVE DEVICES		Invasive devices
5.1. Rule 5 All invasive devices with respect to body orifices, other than surgically invasive devices, which are not intended for connection to an active device or which are intended for connection to a class I active device are classified as: — class I if they are intended for transient use; — class IIa if they are intended for short-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity, in which case they are classified as class I; and — class IIb if they are intended for long-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are classified as class IIa. All invasive devices with respect to body orifices, other than surgically invasive devices, intended for connection to a class IIa, class IIb or class III active device, are classified as class IIa.		Rule 5 4.—(1) All invasive devices with respect to body orifices, other than surgically invasive devices, which are not intended for connection to an active device or which are intended for connection to a Class I active device are classified as— (a) Class I if they are intended for transient use; (b) Class IIa if they are intended for short-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity, in which case they are classified as class I; (c) Class IIb if they are intended for long-term use, except if they are used in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in the nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are classified as class IIa. All invasive devices with respect to body orifices, other than surgically invasive devices, intended for connection to a Class IIa, Class IIb or Class III active device, are classified as Class IIa.

5.2. Rule 6 All surgically invasive devices intended for transient use are classified as class IIa unless they: — are intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as class III; — are reusable surgical instruments, in which case they are classified as class I; — are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as class III; — are intended to supply energy in the form of ionising radiation in which case they are classified as class IIb; — have a biological effect or are wholly or mainly absorbed in which case they are classified as class IIb; or — are intended to administer medicinal products by means of a delivery system, if such administration of a medicinal product is done in a manner that is potentially hazardous taking account of the mode of application, in which case they are classified as class IIb.		Rule 6 (2) All surgically invasive devices intended for transient use are classified as class IIa unless they— (a) are intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as Class III; (b) are reusable surgical instruments, in which case they are classified as class I; (c) are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as Class III; (d) are intended to supply energy in the form of ionising radiation in which case they are classified as Class IIb; (e) have a biological effect or are wholly or mainly absorbed in which case they are classified as Class IIb; or (f) are intended to administer medicinal products by means of a delivery system, if such administration of a medicinal product is done in a manner that is potentially hazardous taking account of the mode of application, in which case they are classified as Class IIb.

5.3. Rule 7 All surgically invasive devices intended for short-term use are classified as class IIa unless they: — are intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as class III; — are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as class III; — are intended to supply energy in the form of ionizing radiation in which case they are classified as class IIb; — have a biological effect or are wholly or mainly absorbed in which case they are classified as class III; — are intended to undergo chemical change in the body in which case they are classified as class IIb, except if the devices are placed in the teeth; or — are intended to administer medicines, in which case they are classified as class IIb.		Rule 7 (3) All surgically invasive devices intended for short-term use are classified as Class IIa unless they— (a) are intended specifically to control, diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with those parts of the body, in which case they are classified as class III; (b) are intended specifically for use in direct contact with the heart or central circulatory system or the central nervous system, in which case they are classified as Class III; (c) are intended to supply energy in the form of ionizing radiation in which case they are classified as Class IIb; (d) have a biological effect or are wholly or mainly absorbed in which case they are classified as Class III; (e) are intended to undergo chemical change in the body in which case they are classified as Class IIb, except if the devices are placed in the teeth; or (f) are intended to administer medicines, in which case they are classified as Class IIb.

5.4. Rule 8 All implantable devices and long-term surgically invasive devices are classified as class IIb unless they: — are intended to be placed in the teeth, in which case they are classified as class IIa; — are intended to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are classified as class III; — have a biological effect or are wholly or mainly absorbed, in which case they are classified as class III; — are intended to undergo chemical change in the body in which case they are classified as class III, except if the devices are placed in the teeth; — are intended to administer medicinal products, in which case they are classified as class III; — are active implantable devices or their accessories, in which cases they are classified as class III; — are breast implants or surgical meshes, in which cases they are classified as class III; — are total or partial joint replacements, in which case they are classified as class III, with the exception of ancillary components such as screws, wedges, plates and instruments; or		Rule 8 (4) All implantable devices and long-term surgically invasive devices are classified as Class IIb unless they— (a) are intended to be placed in the teeth, in which case they are classified as Class IIa; (b) are intended to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are classified as Class III; (c) are intended to undergo chemical change in the body in which case they are classified as Class III, except if the devices are placed in the teeth; (d) are intended to administer medicinal products, in which case they are classified as Class III; (e) are active implantable devices or their accessories, in which case they are classified as Class III; (f) are breast implants or surgical meshes, in which cases they are classified as Class III; (g) are total or partial joint replacements, in which case they are classified as Class III, with the exception of ancillary components such as screws, wedges, plates and instruments; or (h) are spinal disc replacement implants or are implantable devices that come into contact with the spinal column, in which case they are

— are spinal disc replacement implants or are implantable devices that come into contact with the spinal column, in which case they are classified as class III with the exception of components such as screws, wedges, plates and instruments.		classified as Class III with the exception of components such as screws, wedges, plates and instruments.

6. ACTIVE DEVICE		Active devices
6.1. Rule 9 All active therapeutic devices intended to administer or exchange energy are classified as class IIa unless their characteristics are such that they may administer energy to or exchange energy with the human body in a potentially hazardous way, taking account of the nature, the density and site of application of the energy, in which case they are classified as class IIb. All active devices intended to control or monitor the performance of active therapeutic class IIb devices, or intended directly to influence the performance of such devices are classified as class IIb. All active devices intended to emit ionizing radiation for therapeutic purposes, including devices which control or monitor such devices, or which directly influence their performance, are classified as class IIb. All active devices that are intended for controlling, monitoring or directly influencing the performance of active implantable devices are classified as class III.		Rule 9 5.—(1) All active therapeutic devices intended to administer or exchange energy are classified as Class IIa unless their characteristics are such that they may administer energy to or exchange energy with the human body in a potentially hazardous way, taking account of the nature, the density and site of application of the energy, in which case they are classified as Class IIb. (2) All active devices intended to control or monitor the performance of active therapeutic Class IIb devices, or intended directly to influence the performance of such devices are classified as Class IIb. (3) All active devices intended to emit ionizing radiation for therapeutic purposes, including devices which control or monitor such devices, or which directly influence their performance, are classified as Class IIb. (4) All active devices that are intended for controlling, monitoring or directly influencing the performance of active implantable devices are classified as Class III.

6.2. Rule 10 Active devices intended for diagnosis and monitoring are classified as class IIa: — if they are intended to supply energy which will be absorbed by the human body, except for devices intended to illuminate the patient's body, in the visible spectrum, in which case they are classified as class I; — if they are intended to image in vivo distribution of radiopharmaceuticals; or — if they are intended to allow direct diagnosis or monitoring of vital physiological processes, unless they are specifically intended for monitoring of vital physiological parameters and the nature of variations of those parameters is such that it could result in immediate danger to the patient, for instance variations in cardiac performance, respiration, activity of the central nervous system, or they are intended for diagnosis in clinical situations where the patient is in immediate danger, in which cases they are classified as class IIb. Active devices intended to emit ionizing radiation and intended for diagnostic or therapeutic radiology, including interventional radiology devices and devices which control or monitor such devices, or which directly influence their performance, are classified as class IIb.		Rule 10 (5) Active devices intended for diagnosis and monitoring are classified as Class IIa— (a) if they are intended to supply energy which will be absorbed by the human body, except for devices intended to illuminate the patient’s body, in the visible spectrum, in which case they are classified as class I; (b) if they are intended to image in vivo distribution of radiopharmaceuticals; (c) if they are intended to image in vivo distribution of radiopharmaceuticals; or (d) if they are intended to allow direct diagnosis or monitoring of vital physiological processes, unless they are specifically intended for monitoring of vital physiological parameters and the nature of variations of those parameters is such that it could result in immediate danger to the patient, for instance variations in cardiac performance, respiration, activity of the central nervous system, or they are intended for diagnosis in clinical situations where the patient is in immediate danger, in which cases they are classified as Class IIb. (6) Active devices intended to emit ionizing radiation and intended for diagnostic or therapeutic radiology, including interventional radiology devices and devices which control or monitor such devices, or which directly influence their performance, are classified as Class IIb.

6.3. Rule 11 Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class IIa, except if such decisions have an impact that may cause: — death or an irreversible deterioration of a person's state of health, in which case it is in class III; or — a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class IIb. Software intended to monitor physiological processes is classified as class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb. All other software is classified as class I.		Rule 11 (7) Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as Class IIa, except if such decisions have an impact that may cause— (a) death or an irreversible deterioration of a person’s state of health, in which case it is in class III; or (b) a serious deterioration of a person’s state of health or a surgical intervention, in which case it is classified as Class IIb. (8) Software intended to monitor physiological processes is classified as Class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as Class IIb. (9) All other software is classified as Class I.

6.4. Rule 12 All active devices intended to administer and/or remove medicinal products, body liquids or other substances to or from the body are classified as class IIa, unless this is done in a manner that is potentially hazardous, taking account of the nature of the substances involved, of the part of the body concerned and of the mode of application in which case they are classified as class IIb.		Rule 12 (10) All active devices intended to administer or remove medicinal products, body liquids or other substances to or from the body are classified as Class IIa, unless this is done in a manner that is potentially hazardous, taking account of the nature of the substances involved, of the part of the body concerned and of the mode of application in which case they are classified as Class IIb.

6.5. Rule 13 All other active devices are classified as class I.		Rule 13 (11) All other active devices are classified as Class I.

7. SPECIAL RULES		Special rules
7.1. Rule 14 All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, as defined in point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma, as defined in point 10 of Article 1 of that Directive, and that has an action ancillary to that of the devices, are classified as class III.		Rule 14 6.—(1) All devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, as defined in regulation 2(1) of the Human Medicines Regulations 2012, including a medicinal product derived from human blood or human plasma, and that has an action ancillary to that of the devices, are classified as Class III.
7.2. Rule 15 All devices used for contraception or prevention of the transmission of sexually transmitted diseases are classified as class IIb, unless they are implantable or long term invasive devices, in which case they are classified as class III.		Rule 15 (2) All devices used for contraception or prevention of the transmission of sexually transmitted diseases are classified as Class IIb, unless they are implantable or long term invasive devices, in which case they are classified as class III.
7.3. Rule 16 All devices intended specifically to be used for disinfecting, cleaning, rinsing or, where appropriate, hydrating contact lenses are classified as class IIb. All devices intended specifically to be used for disinfecting or sterilising medical devices are classified as class IIa, unless they are disinfecting solutions or washer-disinfectors intended specifically to be used for disinfecting invasive devices, as the end point of processing, in which case they are classified as class IIb.		Rule 16 (3) All devices intended specifically to be used for disinfecting, cleaning, rinsing or, where appropriate, hydrating contact lenses are classified as Class IIb. (4) All devices intended specifically to be used for disinfecting or sterilising medical devices are classified as Class IIa, unless they are disinfecting solutions or washerdisinfectors intended specifically to be used for disinfecting invasive devices, as the end point of processing, in which case they are classified as Class IIb.

This rule does not apply to devices that are intended to clean devices other than contact lenses by means of physical action only.		(5) Rule 16 does not apply to devices that are intended to clean devices other than contact lenses by means of physical action only.

7.4. Rule 17 Devices specifically intended for recording of diagnostic images generated by X-ray radiation are classified as class IIa.		Rule 17 (6) Devices specifically intended for recording of diagnostic images generated by X-ray radiation are classified as Class IIa.
7.5. Rule 18 All devices manufactured utilising tissues or cells of human or animal origin, or their derivatives, which are non-viable or rendered non-viable, are classified as class III, unless such devices are manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable and are devices intended to come into contact with intact skin only.		Rule 18 (7) All devices manufactured utilising tissues or cells of human or animal origin, or their derivatives, which are non-viable or rendered non-viable, are classified as class III, unless such devices are manufactured utilising tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable and are devices intended to come into contact with intact skin only.
7.6. Rule 19 All devices incorporating or consisting of nanomaterial are classified as: — class III if they present a high or medium potential for internal exposure; — class IIb if they present a low potential for internal exposure; and — class IIa if they present a negligible potential for internal exposure.		Rule 19 (8) All devices incorporating or consisting of nanomaterial are classified as— (a) Class III if they present a high or medium potential for internal exposure; (b) Class IIb if they present a low potential for internal exposure; (c) Class IIa if they present a negligible potential for internal exposure.

7.7. Rule 20 All invasive devices with respect to body orifices, other than surgically invasive devices, which are intended to administer medicinal products by inhalation are classified as class IIa, unless their mode of action has an essential impact on the efficacy and safety of		Rule 20 (9) All invasive devices with respect to body orifices, other than surgically invasive devices, which are intended to administer medicinal products by inhalation are classified as lass IIa, unless their mode of action has an essential impact on the efficacy and safety of

the administered medicinal product or they are intended to treat life-threatening conditions, in which case they are classified as class IIb.		the administered medicinal product or they are intended to treat life-threatening conditions, in which case they are classified as Class IIb.
7.8. Rule 21 Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body are classified as: — class III if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose; — class III if they achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body; — class IIa if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities; and — class IIb in all other cases.		Rule 21 (10) Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body are classified as— (a) Class III if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose; (b) Class III if they achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body; (c) Class IIa if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities; (d) Class IIb in all other cases.
7.9. Rule 22 Active therapeutic devices with an integrated or incorporated diagnostic function which significantly determines the patient management by the device, such as closed loop systems or automated external defibrillators, are classified as class III.		Rule 22 (11) Active therapeutic devices with an integrated or incorporated diagnostic function which significantly determines the patient management by the device, such as closed loop systems or automated external defibrillators, are classified as Class III.

Appendix C5 1 OCE General Safety and Performance Requirements Matrix

The following is a list of standards which may be applicable to the OCE system

Standard

1. EN ISO 13485:2016
   Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)
   EN ISO 13485:2016/AC:2018
2. EN 13612:2002
   Performance evaluation of in vitro diagnostic medical devices
   EN 13612:2002/AC:2002
3. EN 13641:2002
   Elimination or reduction of risk of infection related to in vitro diagnostic reagents
4. EN 13975:2003
   Sampling procedures used for acceptance testing of in vitro diagnostic medical devices - Statistical aspects
5. EN 14136:2004
   Use of external quality assessment schemes in the assessment of the performance of in vitro diagnostic examination procedures
6. EN 14254:2004
   In vitro diagnostic medical devices - Single-use receptacles for the collection of specimens, other than blood, from humans
7. EN ISO 14971:2012
   Medical devices - Application of risk management to medical devices (ISO 14971:2007, Corrected version 2007-10-01)
8. EN ISO 15223-1:2016
   Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements (ISO 15223-1:2016, Corrected version 2017-03)
9. EN ISO 18113-1:2011
   In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions and general requirements (ISO 18113-1:2009)
10. EN ISO 18113-2:2011
    In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use (ISO 18113-2:2009)
11. EN ISO 18113-3:2011
    In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 3: In vitro diagnostic instruments for professional use (ISO 18113-3:2009)
12. EN 61010-2-101:2002
    Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment
13. EN 61326-2-6:2006
    Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 2-6: Particular requirements - In vitro diagnostic (IVD) medical equipment
14. EN 62304:2006
    Medical device software - Software life-cycle processes (IEC 62304:2006)
    EN 62304:2006/AC:2008
15. EN 62366:2008
    Medical devices - Application of usability engineering to medical devices

Refer to both the EN 60601 and 61010 family of standard as a supplement for the actual design of the hardware and software

e.g.

BS EN 60601-1:2006 Medical electrical equipment - Part 1: General requirements for basic safety and essential performance (IEC 60601-1:2005)

BS EN 61010-1:2010+A1:2019 Safety requirements for electrical equipment for measurement, control, and laboratory use.

Also

EN 1041:2008 Information supplied by the manufacturer of medical devices

EN ISO 15223-1:2016 Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements (ISO 15223-1:2016, Corrected version 2017-03)

ANNEX I
GENERAL SAFETY AND PERFORMANCE REQUIREMENTS
CHAPTER I
GENERAL REQUIREMENTS

Essential Requirement	A NA	Standard	Supporting Documentation	Location of supporting documentation
1. Devices shall achieve the performance intended by their manufacturer and shall be designed and manufactured in such a way that, during normal conditions of use, they are suitable for their intended purpose. They shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art.	A	IVDR EN ISO 13485:2016 EN ISO 15189:2012 EN ISO 14971:2012/2019 EN 61010-2-101:2002 EN ISO 15223-1:2016 EN 61326-2-6:2006 EN 62304:2006 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	WIRD01 Regulatory Legislative Technical File contents. BSI QA Certificate MD UKAS Certificiate WIRD05 Risk Analysis WIRD07 Classification Rules IVDR WIMPI08 Electrical Safety Testing of Medical Equipment. Symbols used detailed in User guide and technical file Review of EMC checks WIRD12 Software Development Cleaning information retained in the User Guide and technical file.	OCE Technical File held in Q-Pulse Copy held in Q-Pulse Copy held in Q-Pulse OCE Risk Assessment and Classification review held in Q-Pulse See e-Quip record for this device. OCE User Guide and Technical File in Q-Pulse. EMC review in OCE Technical File Software design held in OCE Technical File. OCE USER Guide in Technical File held in Q-Pulse.

Essential Requirement	A NA	Standard	Supporting Documentation	Location of supporting documentation
2. The requirement in this Annex to reduce risks as far as possible means the reduction of risks as far as possible without adversely affecting the benefit-risk ratio.	A	EN ISO 14971:2012/2019	Risk Assement for OCE system	OCE Risk Assessment file held in Q-Pulse
3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall: (a) establish and document a risk management plan for each device; (b) identify and analyse the known and foreseeable hazards associated with each device; (c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; (d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4; (e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, the benefit-risk ratio and risk acceptability; and (f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.	A	EN ISO 14971:2012/2019 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	WIRD05 Risk Analysis WIRD07 Classification Rules IVDR QP20 Reporting and Review of Incidents QP26 Customer Feedback	OCE Risk Assessment and Classification review held in Q-Pulse User guide and technical file for details of information passed to users relating to residual risks

Essential Requirement	A NA	Standard	Supporting Documentation	Location of supporting documentation
4. Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, the manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority: (a) eliminate or reduce risks as far as possible through safe design and manufacture; (b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and (c) provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users. Manufacturers shall inform users of any residual risks.	A	UK Legislation EN ISO 14971:2012/2019 EN 61010-2-101:2002 EN ISO 15223-1:2016 Appropriate parts of EN ISO 18113 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	WIRD01 regulatory legislative technical file contents WIRD05 Risk Analysis WIRD07 Classification Rules IVDR WIMPI08 Electrical Safety Testing of Medical Equipment. Symbols used detailed in User guide and technical file OCE user guide and technical file	Technical File for OCE held in Q-Pulse OCE Risk Assessment and Classification review held in Q-Pulse Review of electrical safety in q-pulse and test results held in e-quip OCE user guide held in q-pulse Both held in q-pulse
5. In eliminating or reducing risks related to use error, the manufacturer shall: (a) reduce as far as possible the risks related to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and (b) give consideration to the technical knowledge, experience, education, training and use environment, where applicable, and the medical and physical conditions of intended users (design for lay, professional, disabled or other users).	A NA A	 EN 62366:2008 EN ISO 14971:2012/2019	 Ergonomics not fully reviewed as this is a prototype device WIRD05 Risk Analysis	 OCE user manual held in Q-Pulse states trained users only to operate the OCE system.

Essential Requirement	A NA	Standard	Supporting Documentation	Location of supporting documentation
6. The characteristics and performance of a device shall not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.	A	EN ISO 14971:2012/2019 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	WIRD05 Risk Analysis Correct use details found in the user manual.	OCE user manual held in Q-Pulse . As this is a prototype device and under development this area needs to be reviewed after each modification or change both hardware and software.
7. Devices shall be designed, manufactured and packaged in such a way that their characteristics and performance during their intended use are not adversely affected during transport and storage, for example, through fluctuations of temperature and humidity, taking account of the instructions and information provided by the manufacturer.	A	IVDR BS EN 60601-1 and BS EN 61010 – and associated standards	OCE Technical File	OCE technical file retained in – Q-Pulse.
8. All known and foreseeable risks, and any undesirable effects shall be minimised and be acceptable when weighed against the evaluated potential benefits to the patients and/or the user arising from the intended performance of the device during normal conditions of use.		EN ISO 14971:2012/2019 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	WIRD05 Risk Analysis. Residual risks detailed in the user manual.	OCE user manual held in Q-Pulse .

CHAPTER II

REQUIREMENTS REGARDING PERFORMANCE, DESIGN AND MANUFACTURE

Essential Requirement 9 Performance characteristics	A NA	Standard	Supporting Documentation	Location of supporting documentation
9.1. Devices shall be designed and manufactured in such a way that they are suitable for the purposes referred to in point (2) of Article 2, as specified by the manufacturer, and suitable with regard to the performance they are intended to achieve, taking account of the generally acknowledged state of the art. They shall achieve the performances, as stated by the manufacturer and in particular, where applicable: (a) the analytical performance, such as, analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and quantitation, measuring range, linearity, cut-off, including determination of appropriate criteria for specimen collection and handling and control of known relevant endogenous and exogenous interference, cross-reactions; and (b) the clinical performance, such as diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, likelihood ratio, expected values in normal and affected populations.	A A	IVDR Specification and testing of the device Appropriate parts of BS EN 61010 and BS EN 60101 EN 13612:2002 UOD and NHST ethics requriements	Technical File especially design specification and tests results. Design and manufacturing documentation detailing how the device meets the specification. Testing of performance will use the relevant parts of 13612. If this is relevant then use 60601 or 61010 family. Ethics approval certificate as proof that checking of the samples done in accordance with UK ethics approval legislation. Design specification details expected performance and sensitivity.	Technical File retained in Q-Pulse. This file contains specification and test results showing how the device meets requirements. The testing specification should also detail how the performance of the device is evaluated and then checked by scanning real biopsy samples and comparing these scans against histopathology reports on same samples. Ethics approval number quoted in the OCE technical files.
9.2. The performance characteristics of the device shall be maintained during the lifetime of the device as indicated by the manufacturer.	A	BS EN 60601 and BS EN 61010 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	Design life given in technical file. Calibration detailed in design file and user information to ensure OCE system maintains performance.	Technical file and user information held in q-Pulse.

Essential Requirement 9 Performance characteristics	A NA	Standard	Supporting Documentation	Location of supporting documentation
9.3. Where the performance of devices depends on the use of calibrators and/or control materials, the metrological traceability of values assigned to calibrators and/or control materials shall be assured through suitable reference measurement procedures and/or suitable reference materials of a higher metrological order. Where available, metrological traceability of values assigned to calibrators and control materials shall be assured to certified reference materials or reference measurement procedures.	A	EN 13612:2002 EN 13975:2003 BS EN 60601 BS EN 61010	The OCE device does not use a calibrator or control materials in the normal sense of IVDDs but test parts. Hence the standards given for IVDD may not be correct and hence need to refer to either 60601 or 61010 standards. The final choice and check to be detailed in the calibration details of the technical file –	Technical file held in Q-Pulse
9.4. The characteristics and performances of the device shall be specifically checked in the event that they may be affected when the device is used for the intended use under normal conditions: (a) for devices for self-testing, performances obtained by laypersons; (b) for devices for near-patient testing, performances obtained in relevant environments (for example, patient home, emergency units, ambulances).	 **NA** NA			

Essential Requirement 10 Chemical, physical and biological properties	A NA	Standard	Supporting Documentation	Location of supporting documentation
10.1. Devices shall be designed and manufactured in such a way as to ensure that the characteristics and performance requirements referred to in Chapter I are fulfilled. Particular attention shall be paid to the possibility of impairment of analytical performance due to physical and/or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected (such as biological tissues, cells, body fluids and micro-organisms), taking account of the intended purpose of the device.	A NA	BS EN 60601 BS EN 61010 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	The OCE does not carry out chemical analysis and does not suffer from incompatibility problems. The user guide details how the biopsy sample is to be handled and presented to the OCE system.	User guide held in q-pulse.
10.2. Devices shall be designed, manufactured and packaged in such a way as to minimise the risk posed by contaminants and residues to patients, taking account of the intended purpose of the device, and to the persons involved in the transport, storage and use of the devices. Particular attention shall be paid to tissues exposed to those contaminants and residues and to the duration and frequency of exposure.	NA		The sample is removed from the patient surgically and then passed for scanning away from the patient. In use there is no contact between the patient and the OCE device.	

Essential Requirement 10 Chemical, physical and biological properties	A NA	Standard	Supporting Documentation	Location of supporting documentation
10.3. Devices shall be designed and manufactured in such a way as to reduce to a level as low as reasonably practicable the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), in accordance with Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council (1), and to substances having endocrine disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified in accordance with the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council (2).	A	BS EN 60601 BS EN 61010 EN ISO 14971:2012/2019	Device has some moving parts plus a sample vibration system. None of the parts move in such a manner as to produce debris. Also the device is not intended to be used with in the patient areas – the operating room. Technical details of these parts given in the manufacturing section of the technical file. A review of the risk of debris from these parts is given in the risk review control by WIRD05 Risk Analysis	Technical details and risk review held in technical file which is retained in Q-Pulse.
10.4. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by the unintentional ingress of substances into the device, taking into account the device and the nature of the environment in which it is intended to be used.	A	BS EN 60601 BS EN 61010 EN ISO 14971:2012/2019	The device has designed with appropriate covers and reviewed by NHS Tayside infection control and found to meet requirments.WIRD05 Risk Analysis	Infection control review contained in OCE technical file – risk review.

Essential Requirement 11 Infection and microbial contamination	A NA	Standard	Supporting Documentation	Location of supporting documentation
11.1. Devices and their manufacturing processes shall be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the user or, where applicable, other persons. The design shall: (a) allow easy and safe handling; (b) reduce as far as possible any microbial leakage from the device and/or microbial exposure during use; and, where necessary (c) prevent microbial contamination of the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen.	A	BS EN 60601 BS EN 61010 EN ISO 14971:2012/2019	Device design risk assessed and reviewed to ensure infection risk to user is reduce to a minimum. User guide and ethics agreements detail how to maintain safety for the user. WIRD05 Risk Analysis	Details held in OCE technical files located in the Q-Pulse system.
11.2. Devices labelled either as sterile or as having a specific microbial state shall be designed, manufactured and packaged to ensure that their sterile condition or microbial state is maintained under the transport and storage conditions specified by the manufacturer until that packaging is opened at the point of use, unless the packaging which maintains their sterile condition or microbial state is damaged.	NA		The device is not delivered or used sterile. Nor used in a specific microbial state.	
11.3. Devices labelled as sterile shall be processed, manufactured, packaged and, sterilised by means of appropriate, validated methods.	NA		The device is not delivered or used sterile.	
11.4. Devices intended to be sterilised shall be manufactured and packaged in appropriate and controlled conditions and facilities.	NA		The device is not delivered or used sterile.	

Essential Requirement 11 Infection and microbial contamination	A NA	Standard	Supporting Documentation	Location of supporting documentation
11.5. Packaging systems for non-sterile devices shall maintain the integrity and cleanliness of the product and, where the devices are to be sterilised prior to use, minimise the risk of microbial contamination; the packaging system shall be suitable taking account of the method of sterilisation indicated by the manufacturer.	NA		No packaging.	
11.6. The labelling of the device shall distinguish between identical or similar devices placed on the market in both a sterile and a non-sterile condition additional to the symbol used to indicate that devices are sterile.			Device not delivered or to be used stereile	

Essential Requirement 12 Devices incorporating materials of biological origin	A NA	Standard	Supporting Documentation	Location of supporting documentation
Where devices include tissues, cells and substances of animal, human or microbial origin, the selection of sources, the processing, preservation, testing and handling of tissues, cells and substances of such origin and control procedures shall be carried out so as to provide safety for user or other person. In particular, safety with regard to microbial and other transmissible agents shall be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This might not apply to certain devices if the activity of the microbial and other transmissible agent are integral to the intended purpose of the device or when such elimination or inactivation process would compromise the performance of the device.	NA		The device does not use such substances.	

Essential Requirement 13. Construction of devices and interaction with their environment	A NA	Standard	Supporting Documentation	Location of supporting documentation
13.1. If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system, shall be safe and shall not impair the specified performances of the devices. Any restrictions on use applying to such combinations shall be indicated on the label and/or in the instructions for use.	NA			
13.2. Devices shall be designed and manufactured in such a way as to remove or reduce as far as possible: (a) the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features; (b) risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature, variations in pressure and acceleration or radio signal interferences; (c) the risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use; (d) the risks associated with the possible negative interaction between software and the IT environment within which it operates and interacts; (e) the risks of accidental ingress of substances into the device; (f) the risk of incorrect identification of specimens and the risk of erroneous results due to, for example, confusing colour and/or numeric and/or character codings on specimen receptacles, removable parts and/or accessories used with devices in order to perform the test or assay as intended; (g) the risks of any foreseeable interference with other devices.	A	BS EN 60601 BS EN 61010 EN ISO 14971:2012/2019	WIRD05 Risk Analysis. Device designed and risks reviewed. Details of how any risks noted are reduced to zero or an acceptable level are detailed in the OCE risk review.	Risk review can be found in the OCE technical file held on Q-Pulse.

Essential Requirement 13. Construction of devices and interaction with their environment	A NA	Standard	Supporting Documentation	Location of supporting documentation
13.3. Devices shall be designed and manufactured in such a way as to minimise the risks of fire or explosion during normal use and in single fault condition. Particular attention shall be paid to devices the intended use of which includes exposure to or use in association with flammable or explosive substances or substances which could cause combustion.	A	BS EN 60601 BS EN 61010 EN ISO 14971:2012/2019 EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	User guide states device not to be used in oxygen rich or in area where flammable gasses are present e.g. anesthetic gases. Also risk review looks at such situations and details how these risks are reduced to an acceptable level.	User guide and risk review held in OCE technical file located in Q-Pulse system,
13.4. Devices shall be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively.	A	EN ISO 14971:2012/2019	Calibration details are given in the user manual and discussed in the design files	User details and desing file held in the OCE technical file held in Q-Pulse system.
13.5. Devices that are intended to be operated together with other devices or products shall be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.	NA		Stand alone device.	
13.6. Devices shall be designed and manufactured in such a way as to facilitate their safe disposal and the safe disposal of related waste substances by users, or other person. To that end, manufacturers shall identify and test procedures and measures as a result of which their devices can be safely disposed after use. Such procedures shall be described in the instructions for use.	A	EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	Disposal information given in the user manual	User manual held in the OCE technical file – Q-Pulses system.
13.7 The measuring, monitoring or display scale (including colour change and other visual indicators) shall be designed and manufactured in line with ergonomic principles, taking account of the intended purpose, users and the environmental conditions in which the devices are intended to be used.	A	EN 13641:2002 EN 1041:2008 EN ISO 15223-1:2016	The display is of the OCE scan results and the way it is displayed has been reviewed by various medical and pathology staff.	See review results in the OCE technical file. File maintained in Q-Pulse.

Essential Requirement 14. Devices with a measuring function	A NA	Standard	Supporting Documentation	Location of supporting documentation
14.1. Devices having a primary analytical measuring function shall be designed and manufactured in such a way as to provide appropriate analytical performance in accordance with point (a) of Section 9.1 of Annex I, taking into account the intended purpose of the device.	NA		Device does not have an analytical function.	
14.2. The measurements made by devices with a measuring function shall be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC (3).	A	Directive as detailed.	The measurements for distance and depth are in SI units. The Elastic measurements are a ratio and hence do not have units.	See OCE technical file held in Q-pulse.

Essential Requirement 15. Protection against radiation	A NA	Standard	Supporting Documentation	Location of supporting documentation
15.1. Devices shall be designed, manufactured and packaged in such a way that exposure of users or other persons to radiation (intended, unintended, stray or scattered) is reduced as far as possible and in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for diagnostic purposes.		BS EN 60601 BS EN 61010 EN ISO 14971:2012/2019	The device has been risk assessed and design to ensure any unintended emissions have been reviewed and reduced to minimum. See risk review for details of these reduction measures.	Risk review detailed in the OCE technical file held in Q-Pulse system
15.2. When devices are intended to emit hazardous, or potentially hazardous, ionizing and/or non-ionizing radiation, they shall as far as possible be: (a) designed and manufactured in such a way as to ensure that the characteristics and the quantity of radiation emitted can be controlled and/or adjusted; and (b) fitted with visual displays and/or audible warnings of such emissions.	NA		Device does is not designed to emit hazardous radiation – ionising or non-ionising.	
15.3. The operating instructions for devices emitting hazardous or potentially hazardous radiation shall contain detailed information as to the nature of the emitted radiation, the means of protecting the user, and on ways of avoiding misuse and of reducing the risks inherent to installation as far as possible and appropriate. Information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure shall also be specified.	NA		Device does is not designed to emit hazardous radiation – ionising or non-ionising.	

Essential Requirement 16. Electronic programmable systems — devices that incorporate electronic programmable systems and software that are devices in themselves.	A NA	Standard	Supporting Documentation	Location of supporting documentation
16.1. Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.	NA			
16.2. For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation.	NA			
16.3. Software referred to in this Section that is intended to be used in combination with mobile computing platforms shall be designed and manufactured taking into account the specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).	NA			
16.3. Software referred to in this Section that is intended to be used in combination with mobile computing platforms shall be designed and manufactured taking into account the specific features of the mobile platform (e.g. size and contrast ratio of the screen) and the external factors related to their use (varying environment as regards level of light or noise).	NA			
16.4. Manufacturers shall set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.	A	EN 62304:2006	WIRD01 Regulatory Legislative Technical File contents. WIRD12 Software Development	See user manual and software information for details of system and other software requirements.

Essential Requirement. 17. Devices connected to or equipped with an energy source	A NA	Standard	Supporting Documentation	Location of supporting documentation
17.1. For devices connected to or equipped with an energy source, in the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks.	NA			
17.2. Devices where the safety of the patient depends on an internal power supply shall be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical. If necessary, such warning or indication shall be given prior to the power supply becoming critical.	NA			
17.3. Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks of creating electromagnetic interference which could impair the operation of the device in question or other devices or equipment in the intended environment.	A	BS EN 60601 BS EN 61010 EN 61326-2-6:2006	WIRD01 Regulatory Legislative Technical File contents. See review of emc and emf interference and immunity risk and methods detailed in the risk analysis and design files.	Held in OCE technical on Q-Pulse.
17.4. Devices shall be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.	A	BS EN 60601 BS EN 61010 EN 61326-2-6:2006	WIRD01 Regulatory Legislative Technical File contents. See review of emc and emf interference and immunity risk and methods detailed in the risk analysis and design files.	Held in OCE technical on Q-Pulse.
17.5. Devices shall be designed and manufactured in such a way as to avoid as far as possible the risk of accidental electric shocks to the user, or other person both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer.	A	BS EN 60601 BS EN 61010	Review of electrical hazards and testing of final device as per WIMPI08 Electrical Safety Testing of Medical Equipment	Held in OCE technical on Q-Pulse.

Essential Requirement. 18. Protection against mechanical and thermal risks	A NA	Standard	Supporting Documentation	Location of supporting documentation
18.1. Devices shall be designed and manufactured in such a way as to protect users and other persons against mechanical risks.	A	BS EN 60601 BS EN 61010	WIRD01 Regulatory Legislative Technical File contents WIRD05 Risk Analysis. Risk assessment of the mechanical design for risk and design information details reduction of mechanical risks.	Risk assessment and design details held in OCE technical file on Q-Pulse
18.2. Devices shall be sufficiently stable under the foreseen operating conditions. They shall be suitable to withstand stresses inherent to the foreseen working environment, and to retain this resistance during the expected lifetime of the devices, subject to any inspection and maintenance requirements as indicated by the manufacturer.	A	BS EN 60601 BS EN 61010	WIRD01 Regulatory Legislative Technical File contents WIRD05 Risk Analysis.	Review of stability undertaken. See details in OCE Technical File
18.3. Where there are risks due to the presence of moving parts, risks due to break-up or detachment, or leakage of substances, then appropriate protection means shall be incorporated. Any guards or other means included with the device to provide protection, in particular against moving parts, shall be secure and shall not interfere with access for the normal operation of the device, or restrict routine maintenance of the device as intended by the manufacturer.	NA			
18.4. Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.	A	BS EN 60601 BS EN 61010	WIRD01 Regulatory Legislative Technical File contents WIRD05 Risk Analysis. No vibration risks found.	Risk assessment review held in OCE Technical File retained in Q-Pulse.
18.5. Devices shall be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means	A	BS EN 60601 BS EN 61010	Noise due to the sample vibration system reviewed. Reduced by changing the	Details of noise reduction held in OCE technical file design section

available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.			vibration device and using sound deadening materials inside the enclosure.	
18.6. Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user or other person has to handle, shall be designed and constructed in such a way as to minimise all possible risks.	A	BS EN 60601 BS EN 61010	Industry standard connectors used and those parts which a user may have to access are detailed in the user manual.	See parts list and user manual held in OCE technical file on Q-Pulse.
18.7. Errors likely to be made when fitting or refitting certain parts which could be a source of risk shall be made impossible by the design and construction of such parts or, failing this, by information given on the parts themselves and/or their housings. The same information shall be given on moving parts and/or their housings where the direction of movement needs to be known in order to avoid a risk.	A	BS EN 60601 BS EN 61010	Any parts which user may have to remove or refit are detailed in the user manual. No dangerous moving parts are accessible Also see risk analysis as per WIRD05 Risk Analysis.	Details retained in OCE technical file held in Q-Pulse
18.8. Accessible parts of devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings shall not attain potentially dangerous temperatures under normal conditions of use.	A	BS EN 60601 BS EN 61010	No parts are intended to generate heat are fitted to the device. Enclosures are fitted and the design is such that any parts which might heat up – electrical power supplies are not accessible or touchable. Also see risk analysis as per WIRD05 Risk Analysis.	See risk review and design details held in OCE technical file on Q-Pulse.

Essential Requirement. 19. Protection against the risks posed by devices intended for self-testing or near-patient testing	A NA	Standard	Supporting Documentation	Location of supporting documentation
19.1. Devices intended for self-testing or near-patient testing shall be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to the intended user and the influence resulting from variation that can be reasonably anticipated in the intended user's technique and environment. The information and instructions provided by the manufacturer shall be easy for the intended user to understand and apply in order to correctly interpret the result provided by the device and to avoid misleading information. In the case of near-patient testing, the information and the instructions provided by the manufacturer shall make clear the level of training, qualifications and/or experience required by the user.	A	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113	User manual states only trained staff to use this device and as it is a prototype under development the procedures detailed in the ethics approval must also be followed.	User manual and ethics apporcal reference held in the OCE technical file maintained in Q-Pulse.
19.2. Devices intended for self-testing or near-patient testing shall be designed and manufactured in such a way as to: (a) ensure that the device can be used safely and accurately by the intended user at all stages of the procedure if necessary after appropriate training and/or information; and (b) reduce as far as possible the risk of error by the intended user in the handling of the device and, if applicable, the specimen, and also in the interpretation of the results.	A	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113	User guide details how the device is to be used. Trained staff to operate the unit only. Plus the use of the device at this time is to determine the actual accuracy of the device.	See User manual in OCE technical file held in Q-Pulse.
19.3. Devices intended for self-testing and near-patient testing shall, where feasible, include a procedure by which the intended user: (a) can verify that, at the time of use, the device will perform as intended by the manufacturer; and (b) be warned if the device has failed to provide a valid result.	A	BS EN 60601 BS EN 61010 EN ISO 14971:2012/2019 EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113	Details of how to check the device given in the user manual plus risk assessment of how results given detailed in risk review.	See OCE technical file for details and risk review.

CHAPTER III

REQUIREMENTS REGARDING INFORMATION SUPPLIED WITH THE DEVICE

The following information must retained in the technical file.

Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
20.1. General requirements regarding the information supplied by the manufacturer Each device shall be accompanied by the information needed to identify the device and its manufacturer, and by any safety and performance information relevant to the user or any other person, as appropriate. Such information may appear on the device itself, on the packaging or in the instructions for use, and shall, if the manufacturer has a website, be made available and kept up to date on the website, taking into account the following:	A	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113	User manual gives relevant details of how to use the device and what the various labels mean and were they are found, The Manufacturing instructions detail were labels will be placed.	See OCE technical file for user manual, labelling information and the manufacturing instructions.
(a) The medium, format, content, legibility, and location of the label and instructions for use shall be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use shall be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams.	A		All Labels will be industry standard and in English.	
(b) The information required on the label shall be provided on the device itself. If this is not practicable or appropriate, some or all of the information may appear on the packaging for each unit. If individual full labelling of each unit is not practicable, the information shall be set out on the packaging of multiple devices.	NA		There is no packaging associated with the device. Only one such OCE device.	

Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(c) Labels shall be provided in a human-readable format and may be supplemented by machine-readable information, such as radio-frequency identification or bar codes.	A		Labels are only human readable.	See OCE technical file for user manual, labelling information and the manufacturing instructions.
(d) Instructions for use shall be provided together with devices. However, in duly justified and exceptional cases instructions for use shall not be required or may be abbreviated if the device can be used safely and as intended by the manufacturer without any such instructions for use.	NA		Only the given user manual is issued.	
(e) Where multiple devices, with the exception of devices intended for self-testing or near-patient testing, are supplied to a single user and/or location, a single copy of the instructions for use may be provided if so agreed by the purchaser who in any case may request further copies to be provided free of charge.	NA		Only one OCE device has been manufactured just now if this changes this requirement will be reviewed.	
(f) When the device is intended for professional use only, instructions for use may be provided to the user in non-paper format (e.g. electronic), except when the device is intended for near-patient testing.	A		Electronic copy of the user manual is held on Q-Pulse.	
(g) Residual risks which are required to be communicated to the user and/or other person shall be included as limitations, contra-indications, precautions or warnings in the information supplied by the manufacturer.	A	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113	These details held in the user manual.	User manual contained in OCE technical file found in Q-Pulse
(h) Where appropriate, the information supplied by the manufacturer shall take the form of internationally recognised symbols, taking into account the intended users. Any symbol or identification colour used shall conform to the harmonised standards or CS. In areas for which no harmonised standards or CS exist, the symbols and colours shall be described in the documentation supplied with the device.	A	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	User manual explains meaning of labels and symbols used. These labels and symbols are industry standard symbols and are also detailed in the labels and symbols part of the technical file.	User manual and labels and symbols used detail contained in OCE technical file found in Q-Pulse. .

Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(i) In the case of devices containing a substance or a mixture which may be considered as being dangerous, taking account of the nature and quantity of its constituents and the form under which they are present, relevant hazard pictograms and labelling requirements of Regulation (EC) No 1272/2008 shall apply. Where there is insufficient space to put all the information on the device itself or on its label, the relevant hazard pictograms shall be put on the label and the other information required by Regulation (EC) No 1272/2008 shall be given in the instructions for use.	NA		OCE system does not use such substances or mixtures	
(j) The provisions of Regulation (EC) No 1907/2006 on the safety data sheet shall apply, unless all relevant information, as appropriate, is already made available in the instructions for use.	NA			

Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
20.2. Information on the label The label shall bear all of the following particulars:	A	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	The manufacturing documentation details the information labels to be placed on the OCE system to enable the device to be identified as detailed in this section.	Details of labels and the information they contain are given in the labels section of the of the OCE technical file found in Q-Pulse.
(a) the name or trade name of the device;	A			
(b) the details strictly necessary for a user to identify the device and, where it is not obvious for the user, the intended purpose of the device;	A			
(c) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business;	A			
(d) if the manufacturer has its registered place of business outside the Union, the name of its authorised representative and the address of the registered place of business of the authorised representative;	NA			
	A			

(e) an indication that the device is an in vitro diagnostic medical device, or if the device is a 'device for performance study', an indication of that fact; (f) the lot number or the serial number of the device preceded by the words LOT NUMBER or SERIAL NUMBER or an equivalent symbol, as appropriate; (g) the UDI carrier as referred to in Article 24 and Part C of Annex VI; (h) an unambiguous indication of the time limit for using the device safely, without degradation of performance, expressed at least in terms of year and month and, where relevant, the day, in that order; (i) where there is no indication of the date until when it may be used safely, the date of manufacture. This date of manufacture may be included as part of the lot number or serial number, provided the date is clearly identifiable;	A NA NA A			
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(j) where relevant, an indication of the net quantity of contents, expressed in terms of weight or volume, numerical count, or any combination of thereof, or other terms which accurately reflect the contents of the package; (k) an indication of any special storage and/or handling condition that applies; (l) where appropriate, an indication of the sterile state of the device and the sterilisation method, or a statement indicating any special microbial state or state of cleanliness; (m) warnings or precautions to be taken that need to be brought to the immediate attention of the user of the device or to any other person. This information may be kept to a minimum in which case more detailed information shall appear in the instructions for use, taking into account the intended users;	NA A NA A	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	Device not delivered nor shipped hence this information not required.. Storage details held in the user manual. Not a sterile device nor used sterile. Warning labels detailed in the user manual. Position of labels detailed in the labels section of OCE technical file and the manufacturing instructions.	See OCE technical file for user manual, labelling information and the manufacturing instructions.

(n) if the instructions for use are not provided in paper form in accordance with point (f) of Section 20.1, a reference to their accessibility (or availability), and where applicable the website address where they can be consulted; (o) where applicable, any particular operating instructions; (p) if the device is intended for single use, an indication of that fact. A manufacturer's indication of single use shall be consistent across the Union; (q) if the device is intended for self-testing or near-patient testing, an indication of that fact; (r) where rapid assays are not intended for self-testing or near-patient testing, the explicit exclusion hereof;	A A NA A NA		A copy of user manual given but an indication of electronic copy given on label on OCE system, Operating information given in the user manual Not a single use device. User manual states for near patient testing Not such a device.	
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(s) where device kits include individual reagents and articles that are made available as separate devices, each of those devices shall comply with the labelling requirements contained in this Section and with the requirements of this Regulation; (t) the devices and separate components shall be identified, where applicable in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components. As far as practicable and appropriate, the information shall be set out on the device itself and/or, where appropriate, on the sales packaging; (u) the label for devices for self-testing shall bear the following particulars: (i) the type of specimen(s) required to perform the test (e.g. blood, urine or saliva);	A A NA A NA	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	The Glass slides for holding the biopsy sample Batch information of the glass slides to be retained to allow tractability to tested biopsy sample. OCE system is not for self-testing. Detailed in the user manual	See OCE technical file for user manual, labelling information and the manufacturing instructions.

(ii) the need for additional materials for the test to function properly; (iii)contact details for further advice and assistance. The name of devices for self-testing shall not reflect an intended purpose other than that specified by the manufacturer.	A		Unit does not use additional test materials. Contact details for help given in the user manual.	
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
20.3. Information on the packaging which maintains the sterile condition of a device ('sterile packaging'): The following particulars shall appear on the sterile packaging: (a) an indication permitting the sterile packaging to be recognised as such, (b) a declaration that the device is in a sterile condition, (c) the method of sterilisation, (d) the name and address of the manufacturer, (e) a description of the device, (f) the month and year of manufacture,	NA	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	Device not delivered sterile nor used in sterile state.	

(g) an unambiguous indication of the time limit for using the device safely, expressed at least in terms of year and month and, where relevant, the day, in that order, (h) an instruction to check the instructions for use for what to do if the sterile packaging is damaged or unintentionally opened before use.				
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
20.4. Information in the instructions for use 20.4.1. The instructions for use shall contain all of the following particulars: (a) the name or trade name of the device; (b) the details strictly necessary for the user to uniquely identify the device; (c) the device's intended purpose: (i) what is detected and/or measured; (ii) its function (e.g. screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic); (iii)the specific information that is intended to be provided in the context of: — a physiological or pathological state; — congenital physical or mental impairments; — the predisposition to a medical condition or a disease;	A	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	User manual	See OCE technical file for user manual, labelling information and the manufacturing instructions.

— the determination of the safety and compatibility with potential recipients; — the prediction of treatment response or reactions; — the definition or monitoring of therapeutic measures; (iv) whether it is automated or not; (v) whether it is qualitative, semi-quantitative or quantitative; (vi) the type of specimen(s) required; (vii) where applicable, the testing population; and (viii) for companion diagnostics, the International Non-proprietary Name (INN) of the associated medicinal product for which it is a companion test. (d) an indication that the device is an in vitro diagnostic medical device, or, if the device is a 'device for performance study', an indication of that fact;				
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(e) the intended user, as appropriate (e.g. self-testing, near patient and laboratory professional use, healthcare professionals); (f) the test principle; (g) a description of the calibrators and controls and any limitation upon their use (e.g. suitable for a dedicated instrument only); (h) a description of the reagents and any limitation upon their use (e.g. suitable for a dedicated instrument only) and the composition of the reagent product by nature and amount or concentration of the active ingredient(s) of the reagent(s) or kit as well as a statement, where appropriate, that the device contains other ingredients which might influence the measurement; (i) a list of materials provided and a list of special materials required but not provided; (j) for devices intended for use in combination with or installed with or connected to other devices and/or general purpose equipment:	A A NA NA A NA	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	Detailed in the user manual. Detailed in the user manual. No such calibrators and control used with the OCE system. No reagents used. Detial of how to make the silicon/agar base and glass slide. Not used in combination with other devices.	See OCE technical file for user manual, labelling information and the manufacturing instructions.

— information to identify such devices or equipment, in order to obtain a validated and safe combination, including key performance characteristics, and/or — information on any known restrictions to combinations of devices and equipment. (k) an indication of any special storage (e.g. temperature, light, humidity, etc.) and/or handling conditions which apply; (l) in-use stability which may include the storage conditions, and shelf life following the first opening of the primary container, together with the storage conditions and stability of working solutions, where this is relevant;	A NA		Storage instructions given in the user manual. No stability issues with the OCE device.	

Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(m) if the device is supplied as sterile, an indication of its sterile state, the sterilisation method and instructions in the event of the sterile packaging being damaged before use;	NA	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	OCE not supplied sterile.	See OCE technical file for user manual, labelling information and the manufacturing instructions.
(n) information that allows the user to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the device. That information shall cover, where appropriate:	A		All this information contained in the user manual.	
(i) warnings, precautions and/or measures to be taken in the event of malfunction of the device or its degradation as suggested by changes in its appearance that may affect performance,	A			
(ii) warnings, precautions and/or measures to be taken as regards the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature,	A			
(iii) warnings, precautions and/or measures to be taken as regards the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or other procedures such as electromagnetic interference emitted by the device affecting other equipment,	A			
(iv) precautions related to materials incorporated into the device that contain or consist of CMR substances, or endocrine disrupting substances or that could result in sensitisation or an allergic reaction by the patient or user,	NA		No such materials contained in the OCE system,	
(v) if the device is intended for single use, an indication of that fact. A manufacturer's indication of single use shall be consistent across the Union,	NA		No a single use device.	
(vi) if the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, decontamination, packaging and, where appropriate, the validated method of re-sterilisation. Information shall be provided to identify when the	A			

device should no longer be reused, such as signs of material degradation or the maximum number of allowable reuses;				

Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(o) any warnings and/or precautions related to potentially infectious material that is included in the device;	NA	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	No such material contained in the OCE.	See OCE technical file for user manual, labelling information and the manufacturing instructions.
(p) where relevant, requirements for special facilities, such as a clean room environment, or special training, such as on radiation safety, or particular qualifications of the intended user;	A		The user to be trained in interpretation of the scans.	
(q) conditions for collection, handling, and preparation of the specimen;	A		Sample collection is a surgical procedure – only undertaken by trained surgeons.	
(r) details of any preparatory treatment or handling of the device before it is ready for use, such as sterilisation, final assembly, calibration, etc., for the device to be used as intended by the manufacturer;	A		Device preparation detailed in user manual – basically is it clean and does it setup correctly.	
(s) the information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant:	A		Setup and peruse checks detailed in the user manual.	
— details of the nature, and frequency, of preventive and regular maintenance, including cleaning and disinfection;				
— identification of any consumable components and how to replace them;				
— information on any necessary calibration to ensure that the device operates properly and safely during its intended lifetime;				
— methods for mitigating the risks encountered by persons involved in installing, calibrating or servicing devices.				
(t) where applicable, recommendations for quality control procedures;	A		OCE system calibration detailed in the user manual.	
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation

(u) the metrological traceability of values assigned to calibrators and control materials, including identification of applied reference materials and/or reference measurement procedures of higher order and information regarding maximum (self-allowed) batch to batch variation provided with relevant figures and units of measure;	NA	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	Material calibrators and the like not used with the OCE.	See OCE technical file for user manual, labelling information and the manufacturing instructions.
(v) assay procedure including calculations and interpretation of results and where relevant if any confirmatory testing shall be considered; where applicable, the instructions for use shall be accompanied by information regarding batch to batch variation provided with relevant figures and units of measure;	NA		There is no assay involved with the OCE.	
(w) analytical performance characteristics, such as analytical sensitivity, analytical specificity, trueness (bias), precision (repeatability and reproducibility), accuracy (resulting from trueness and precision), limits of detection and measurement range, (information needed for the control of known relevant interferences, cross-reactions and limitations of the method), measuring range, linearity and information about the use of available reference measurement procedures and materials by the user;	A		How to review the scan information is by training and presentation of results is detailed in the user manual	
(x) clinical performance characteristics as defined in Section 9.1 of this Annex;	A		Performance defined in the user manual and OCE specification.	
(y) the mathematical approach upon which the calculation of the analytical result is made;	A		Defined in the OCE specification and outlined in the user manual.	
(z) where relevant, clinical performance characteristics, such as threshold value, diagnostic sensitivity and diagnostic specificity, positive and negative predictive value;	A		Defined in the user manual.	
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(aa) where relevant, reference intervals in normal and affected populations;	NA	EN 1041:2008 EN ISO 15223-1:2016	Not used in this manner.	See OCE technical file for user manual, labelling information

(ab) information on interfering substances or limitations (e.g. visual evidence of hyperlipidaemia or haemolysis, age of specimen) that may affect the performance of the device; (ac) warnings or precautions to be taken in order to facilitate the safe disposal of the device, its accessories, and the consumables used with it, if any. This information shall cover, where appropriate: (i) infection or microbial hazards, such as consumables contaminated with potentially infectious substances of human origin; (ii) environmental hazards such as batteries or materials that emit potentially hazardous levels of radiation); (iii)physical hazards such as explosion. (ad) the name, registered trade name or registered trade mark of the manufacturer and the address of its registered place of business at which he can be contacted and its location be established, together with a telephone number and/or fax number and/or website address to obtain technical assistance; (ae) date of issue of the instructions for use or, if they have been revised, date of issue and identifier of the latest revision of the instructions for use, with a clear indication of the introduced modifications; (af) a notice to the user that any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established;	NA A A NA A A A A	EN ISO 18113 and other standards for symbols	No interfering substances Disposal information contained in user manual. Disposal of contaminated slides detailed in user manual No such material with the OCE Such risk detailed in the user instructions. User manual contain these details. Issue and revision information contained in the user manual. Feedback instruction detailed in the user manual.	and the manufacturing instructions.
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(ag) where device kits include individual reagents and articles that may be made available as separate devices, each of these devices shall comply with the instructions for use requirements contained in this Section and with the requirements of this Regulation;	NA	EN 1041:2008 EN ISO 15223-1:2016 EN ISO 18113 and other standards for symbols	OCE does not user reagents and similar materials.	

(ah) for devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorised access, necessary to run the software as intended.	NA		OCE does not contain such systems.	
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
20.4.2 In addition, the instructions for use for devices intended for self-testing shall comply with all of the following principles: (a) details of the test procedure shall be given, including any reagent preparation, specimen collection and/or preparation and information on how to run the test and interpret the results; (b) specific particulars may be omitted provided that the other information supplied by the manufacturer is sufficient to enable the user to use the device and to understand the result(s) produced by the device; (c) the device's intended purpose shall provide sufficient information to enable the user to understand the medical context and to allow the intended user to make a correct interpretation of the results; (d) the results shall be expressed and presented in a way that is readily understood by the intended user; (e) information shall be provided with advice to the user on action to be taken (in case of positive, negative or indeterminate result), on the test limitations and on the possibility of false positive or false negative result. Information shall also be provided as to any factors that can affect the test result such as age, gender, menstruation, infection, exercise, fasting, diet or medication; (f) the information provided shall include a statement clearly directing that the user should not take any decision of medical relevance without first consulting the appropriate healthcare professional, information on disease effects and prevalence, and, where available, information specific to the Member State(s) where the	NA		OCE system is not for self-testing	

device is placed on the market on where a user can obtain further advice such as national helplines, websites;				
Essential Requirement. 20. Label and instructions for use	A NA	Standard	Supporting Documentation	Location of supporting documentation
(g) for devices intended for self-testing used for the monitoring of a previously diagnosed existing disease or condition, the information shall specify that the patient should only adapt the treatment if he has received the appropriate training to do so.	NA		The OCE system is not for self-testing.	

Appendix C5 2 Risk Classification For the OCE System

Risk Classification for OCE system using the M&H work instruction.

Implementation rules

1.—(1) Application of the classification rules must be governed by the intended purpose of the devices. - ***The device is intended to scan prostrate biopsy samples to determine if they contain possible cancerous cells or growths***

(2) If the device in question is intended to be used in combination with another device, the classification rules must apply separately to each of the devices. - ***The OCE is a standalone device.***

(3) Accessories for an in vitro diagnostic medical device must be classified in their own right separately from the device with which they are used. - ***The OCE has no accessories.***

(4) Software which—

(a) drives a device or influences the use of a device, must fall within the same class as the device;

(b) is independent of any other device, must be classified in its own right.

The software used is an integral component of the OCE system.

(5) Calibrators intended to be used with a device must be classified in the same class as the device. - ***The calibration devices are physical devices and hence not required to meet this point.***

(6) Control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes must be classified in the same class as the device. - ***No such material used with the OCE system***

(7) The manufacturer must take into consideration all classification and implementation rules in order to establish the proper classification for the device. - ***Only one classification rule applies.***

(8) Where a manufacturer states multiple intended purposes for a device, and as a result the device falls into more than one class, it must be classified in the higher class. - ***The OCE system is intended to perform a single task as detailed in one 1-(1) above.***

(9) If several classification rules apply to the same device, the rule resulting in the higher classification must apply.- ***Single rule applies.***

(10) Each of the classification rules must apply to first line assays, confirmatory assays and supplemental assays. - ***The OCE does not use assays to perform its analysis.***

Classification rules

Rule 1 ***NOT APPLICABLE***

2.—(1) Devices intended to be used for the following purposes are classified as Class D—

(a) detection of the presence of, or exposure to, a transmissible agent in blood, blood components, cells, tissues or organs, or in any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration;

(b) detection of the presence of, or exposure to, a transmissible agent that causes a life-threatening disease with a high or suspected high risk of propagation;

(a) (c)determining the infectious load of a life-threatening disease where monitoring is critical in the process of patient management.

Rule 2 ***NOT APPLICABLE***

(2) Devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as class C, except when intended to determine any of the following markers—

(a) ABO system [A (ABO1), B (ABO2), AB (ABO3)];

(b) Rhesus system [RH1 (D), RHW1, RH2 (C), RH3 (E), RH4 (c), RH5 (e)];

(c) Kell system [Kel1 (K)];

(d) Kidd system [JK1 (Jka), JK2 (Jkb)];

(e) Duffy system [FY1 (Fya), FY2 (Fyb)];

in which case they are classified as Class D.

Rule 3 ***APPLICABLE see point (h).***

(3) Devices are classified as Class C if they are intended—

(a) for detecting the presence of, or exposure to, a sexually transmitted agent;

(b) for detecting the presence in cerebrospinal fluid or blood of an infectious agent without a high or suspected high risk of propagation;

(c) for detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested, or to the individual's offspring;

(d) for pre-natal screening of women in order to determine their immune status towards transmissible agents;

(e) for determining infective disease status or immune status, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;

(f) to be used as companion diagnostics;

(g) to be used for disease staging, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;

(h) to be used in screening, diagnosis, or staging of cancer;

(i) for human genetic testing;

(j) for monitoring of levels of medicinal products, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring;

(k) for management of patients suffering from a life-threatening disease or condition;

(l) for screening for congenital disorders in the embryo or foetus;

(m) for screening for congenital disorders in new-born babies where failure to detect and treat such disorders could lead to life-threatening situations or severe disabilities.

Rule 4 ***NOT APPLICABLE***

(4) Devices intended for self-testing are classified as Class C, except for devices testing the following which are classified in Class D—

(a) the detection of pregnancy;

(b) fertility testing;

(c) for determining cholesterol level;

(d) for the detection of glucose, erythrocytes, leucocytes and bacteria in urine.

(5) Devices intended for near-patient testing are classified in their own right.
Device is class C due to Rule 3 point (h)

Rule 5 ***NOT APPLICABLE***

(6) The following devices are classified as Class A—

(a) products for general laboratory use, accessories which possess no critical characteristics, buffer solutions, washing solutions, and general culture media and histological stains, intended by the manufacturer to make them suitable for in vitro diagnostic procedures relating to a specific examination;

(b) instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures;

(c) specimen receptacles.

Rule 6 ***NOT APPLICABLE***

Devices not covered by the above-mentioned classification rules are classified as Class B.

Rule 7 ***NOT APPLICABLE***

Devices which are controls without a quantitative or qualitative assigned value are classified as Class B.

Classification Review Summary

Classification Rule Review

RULE	Details of why are rule applies or not	Rule Review Result – A or N/A
1	Does not apply as device not used for the purposes of determining infection load or infection transmissibility.	N/A
2	The devices is not used for compatibility checking	N/A
3	The device is used for screening and in the diagnosis of cancer.	A – Class C
4	Device is not intended for self-testing but near patient testing as per Rule 4 point (5) hence rule 3 still applies.	N/A
5	The device is a device in itself.	N/A
6	Device is cover by Rule 3	N/A
7	Device is cover by Rule 3	N/A

Final Review Classification – THIS IVDD DEVICE IS A CLASS C DEVICE.

Only one classification rule applies to this device due to its intended purpose.

Summary

The device is intended to scan prostrate biopsy samples to determine if they contain possible cancerous cells or growths. The device is intended for near patient testing. Rule 3 point (h) applies hence the Class C determination.

The OCE is a standalone device.

The OCE has no accessories.

The software used is an integral component of the OCE system.

The calibration devices are physical devices and hence not required to meet this point.

No control materials are used with the OCE system

Only one classification rule applies.

The OCE system is intended to perform a single task - analysis of biopsy samples.

The OCE does not use assays to perform its analysis.

Appendix C5 3 IVDD Exemption Regulations UK legislation Only

IVDD Exemption parts UK legislation

UK legislation 2019 No. 791

EXITING THE EUROPEAN UNION CONSUMER PROTECTION

The Medical Devices (Amendment etc.) (EU Exit) Regulations

2019 - Made 1st April 2019

The section

PART 3

New part IX of the Medical Devices Regulations

11. After regulation 135 (as inserted by regulation 10) insert—

"PART IX

The rights, powers, liabilities, obligations, restrictions, remedies and procedures recognised under the in vitro diagnostic Medical Devices Regulation (see regulation 4P)

... text deleted …....

Making available on the market and putting into service of devices, obligations of economic operators, CE marking

Placing on the market and putting into service

140.—(1) A device to which this Part applies may be placed on the market or put into service only if it complies with this Part when duly supplied and properly installed, maintained and used in accordance with its intended purpose.

(2) A device to which this Part applies must meet the general safety and performance requirements set out in Schedule 17 which apply to it, taking into account its intended purpose.

(3) Demonstration of conformity with the general safety and performance requirements must include a performance evaluation in accordance with regulation 167.

(4) Devices that are manufactured and used within health institutions, with the exception of devices for performance studies, must be considered as having been put into service.

(5) With the exception of the relevant general safety and performance requirements set out in Schedule 17, the requirements of this Part do not apply to a device which is manufactured and used only within a health institution, provided that all of the following conditions are met—

(a) the device is not transferred to another legal entity;

(b) manufacture and use of the devices occur under appropriate quality management systems;

(c) the laboratory of the health institution is compliant with standard EN ISO 15189 and, where applicable, provisions regarding accreditation;

(d) the health institution justifies in its documentation that the specific needs of the target patient group cannot be met, or cannot be met at the appropriate level of performance by an equivalent device available on the market;

(e) on request from the Secretary of State, the health institution provides the Secretary of State with information (which must include justification for its manufacturing, modification and use of such devices) on the use of the device to the Secretary of State;

(f) the health institution draws up a declaration which it must make publicly available,

including—

(i) the name and address of the manufacturing health institution;

(ii) the details necessary to identify the devices;

(iii) a declaration that the device meets the general safety and performance requirements set out in Schedule 17 and, where applicable, information on which requirements are not fully met and a reasoned justification for not meeting those requirements;

(g) for Class D devices (and for other classes of device in accordance with the rules set out in Schedule 23) the health institution draws up a document which makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices and the intended purpose, and which is sufficiently detailed to enable the Secretary of State to ascertain that the general safety and performance requirements set out in Schedule 17 are met;

(h) the Secretary of State may apply the provisions of sub-paragraph (g) also to Class A, B or C devices in accordance with the rules set out in Schedule 23;

(i) the health institution must take all necessary measures to ensure that all devices are manufactured in accordance with the document referred to in sub-paragraph (g);

(j) the health institution reviews experience gained from clinical use of the devices an takes all necessary corrective actions.

(6) The Secretary of State may require a health institution which has complied with paragraph (5) to submit to the Secretary of State any further relevant information about such devices which it has manufactured and used.

(7) The Secretary of State may restrict the manufacture and use of a specified type of device manufactured in accordance with paragraph (5) and, for the purposes of considering such a restriction, must be permitted access to inspect the activities of the health institutions.

(8) Paragraph (5) does not apply to the devices that are manufactured on an industrial scale.

Appendix C5 4 Declaration of Conformance OCE System

The Department of Medical Physics, NHS Tayside, declares that the Optical Coherence Elastography system meets the exemption requirements detailed in

Paragraph 140, 'Placing on the market and putting into service' part (5)

UK legislation 2019 No. 791, Exiting the European Union Consumer Protection, The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 - Made 1st April 2019.

The OCE system has been design and developed under an accredited BS EN ISO 1345:2016 quality assurance system BSI certificate MD 77843.

Justification for the manufacture of the OCE system.

The OCE system has been manufactured to determine the feasibility using Optical Coherence Tomography coupled with vibrational Elastography to review biopsy samples for the presence of cancerous nodules. No such device exists on the market at present. If such a device were available the time take to review such samples would be reduce from 3 days to one hour. This reduction in the time to review a biopsy sample may allow a surgeon to perform the biopsy operation, review the scan results and operate on the cancerous region without the patient leaving the operation room and having to return another day.

The device is identified in the NHS Tayside medical assessment management system by the following equipment asset number

OCE scanning part	MP
Power amplifier	MP
Signal generator	MP

Photographs of the OCE system are contained in the device description part of the OCE Technical File. Once such photograph is presented below to assist in identifying the OCE system.

The technical file containing full details of the OCE system including its design, manufacture, risk and hazard analysis and user information is retained in the Medical Physics Q-Pulse system – 'OCE Technical File'. This file also contains a full review of the General Safety and Performance Requirements as set out in Schedule 17 of the above UK legislation..

The General Safety and Performance Requirements have been reviewed against the following standards –

Standard	Name
EN ISO 13485:2016 (ISO 13485:2016) EN ISO 13485:2016/AC:2018	Medical devices - Quality management systems - Requirements for regulatory purposes
EN 13612:2002 EN 13612:2002/AC:2002	Performance evaluation of in vitro diagnostic medical devices
EN 13641:2002	Elimination or reduction of risk of infection related to in vitro diagnostic reagents
EN ISO 14971:2012 (ISO 14971:2007, Corrected version 2007-10-01) EN ISO 14971:2019	Medical devices - Application of risk management to medical devices
EN ISO 15223-1:2016 (ISO 15223-1:2016, Corrected version 2017-03)	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements
EN ISO 18113-1:2011 (ISO 18113-1:2009)	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: Terms, definitions and general requirements
EN ISO 18113-2:2011 (ISO 18113-2:2009)	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 2: In vitro diagnostic reagents for professional use
EN ISO 18113-3:2011	In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 3: In vitro diagnostic instruments for professional use (ISO 18113-3:2009)
EN 61010-2-101:2002	Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment
EN 61326-2-6:2006	Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 2-6: Particular requirements - In vitro diagnostic (IVD) medical equipment
EN 62304:2006 (IEC 62304:2006) EN 62304:2006/AC:2008	Medical device software - Software life-cycle processes (IEC 62304:2006) EN 62304:2006/AC:2008
EN 62366:2008	Medical devices - Application of usability engineering to medical devices
EN 1041:2008 +A1:201	Information supplied by the manufacturer of medical devices
BS EN 60601-1:2006	Medical electrical equipment - Part 1: General requirements for basic safety and essential performance (IEC 60601-1:2005)
BS EN 61010-1:2010+A1:2019	Safety requirements for electrical equipment for measurement, control, and laboratory use.

Note that the design of the OCE system refers to both the EN 60601 and 61010 family of standard as a supplement for the actual design of the hardware and software

The following standards have not been used as the device does not test or produce results from the study of chemical reactions.

EN 13975:2003	Sampling procedures used for acceptance testing of in vitro diagnostic medical devices - Statistical aspects
EN 14136:2004	Use of external quality assessment schemes in the assessment of the performance of in vitro diagnostic examination procedures
EN 14254:2004	In vitro diagnostic medical devices - Single-use receptacles for the collection of specimens, other than blood, from humans

Appendix C5 5 Initial risk analysis for the OCE system

This appendix details the initial draft hazard and risk assessment for the OCE system.

Hazard and Risk Assessment, Review and Reduction Report OCE System

Device outline

The OCE system is being developed to determine the feasibility to use combined optical coherence and elastography to determine if biopsy sample contain cancerous nodes. The initial biopsy samples being tested are from the prostrate.

The device consists of

1. An optical coherence system using a solid state laser as the light source

2. A sample vibration system driven by an external amplifier driven from a signal generator. The sample vibration system is mounted on an x, y, z positioning system.

3. A control PC, digital and analogue input output cards used to control the OCE system and to digitise the signal from the optical coherence microscope.

4. A pneumatic anti-vibration table

All parts of the system, apart from the power amplifier and the signal generator, are contained within a wheeled enclosure. The amplifier and the signal generator are on a separate small table.

Application of the device.

The device will be used to scan prostrate samples of approximately 20mm x 2 mm or less. The samples taken during routine prostrate examination within Ninewells Hospital Urology theatre. The samples are passed from theatre to the location of the OCE system for scanning and then returned to theatre. The samples are the passed to Histopathology for review and reporting.

The results from OCE scanning are compared to those from Histopathology to determine the accuracy of the OCE results.

Policy for the determining the acceptable level of risk/hazard.

The device should not present any residual risk over and above that expected from an item of laboratory equipment used to optically scan biopsy samples e.g. no radiation hazards, no hazards from the mechanical properties of the OCE device, no residual hazards due to scanning a biopsy sample, no electrical hazards..

The Verification Plan

The output from the final risk and hazard risk analysis will be reviewed by the academic supervisor, supervising clinical/medical staff and medical staff. The risk and hazard analysis may need to be revised in light of comments from these review due to new risk or hazards being highlighted or comments made on the risk and hazards detailed in the analysis.

Only when all parties carrying out the verification of the risk and hazard risk analysis, can this analysis be deemed complete. The statement informing that the use of the device out weights any residual risk or hazards will be signed by both the academic lead and senior medical physics clinical engineered or scientist.

Allocation of responsibility

Lead academic developer schedule review meeting

Other academic developers to attend meetings as required.

M&H quality representative to assist/guide in the review process

M&H technical staff to act as independent experts

Risk/hazard analysis review scope and scheduling

The reviews will look at all possible risk or hazards associated with the device, its development and manufacture, its use, the users and location of use. The reviews may include risk or hazards foreseen if the device is made commercially, if the results are to be used medically or those arising from possible extensions of use. The reviews should also look at the risk to the samples due to the actually scanning process and the journey the sample takes from patient to final reporting.

Documentation to be produced

Each review and risk/hazard analysis discussion will be documented and retained.

The output of the final risk/hazard review and any comments from the reviews on this by academic lead, clinical lead and medical physics will be retained.

The gathering and review of in use, post manufacture or production data for the OCE system. The data to be retained with the associated risk/hazard analysis. Copies of all feedback received by users or interested parties will be retained on Q-Pulse attached to the relevant Action Form.

Controls to ensure any data or feedback relating to the OCE system is correctly recorded and reported to the M&H quality system. This will be achieved by ensuring the E-Quip entry for the OCE system and associated power amplifier and signal generator has the manufacturer noted as Medical Physics – UOD. This will highlight to staff that this is an in-house manufactured device and problems with the device should be flagged to the quality system.

Each year a review of the feedback and in use data relating to the OCE system will be made available to notified bodies or regulatory authority (MHRA/HFS). The need and contents of this review will be added to WI RD 14 – Notified / Regulatory Review Reports.

Risk/Hazard reviews will be retained with the Technical File for the OCE system – maintained on Q-Pulse.

Action forms relating to feedback and in use data are retained on Q-Pulse

Reviews for external bodies are retained in the Technical File for the OCE system.

E-Quip is the asset management system used by Medical Physics. All details of equipment repair and service are retained on this system.

Q-Pulse and e-Quip are accessed via appropriate login and maintained on NHS Tayside services.

Hazard/Risk identification Form.

Session/Date	Hazard Type	Hazard Description
1 dd/mm/yyyy		
	Acoustic noise	The sample vibration system is noisy. Is the noise above recommended HSE levels.
	Weight	The power amplifier is about 5 Kg. Not secure to table.
	Weight	The main body of the OCE is over 40Kg. Stability.
	Weight	Mounting of both PC and Touchscreen.
	Motion	Are braked castors fitted on the OCE main body and the table for the power amplifier and signal generator.
	electrical / electricity	Check electrical layout and current capabilities of the wiring.
	Moving parts	Safety of motorised XYZ position controller for sample vibration system.
	Sample holder	Is it biocompatible with the biopsy sample? Do the user instructions inform use once only
	Sample holder	Does the sample holder material cause artefacts on the scanned image?
	User instructions	Full reviewed? Contain all the relevant safety information and user instructions.
	Cleaning instructions	Reviewed by infection control? Do the instructions state clean after use.
	Cleaning instructions	These detail full the action to take if the sample or sample fluids falls into the OCE scanning area.
	electrical / electricity	Only trained personnel to carry out repairs on the unit and they must ensure safety from electric shock risks

	Biological hazards	Do the user instructions state no samples to be left inside the OCE after use?
	magnetic fields e.g. MRI	Device is not MRI compatible.
	Anaesthetic gases	Device is not to be used in an explosion risk area – oxygen enriched or with anaesthetic gases present.

Review of Example Hazards List

The example listing of hazards and risks was reviewed those deemed not applicable have been crossed out

Acoustic energy

~~Infrasound,~~

~~produce high sound pressure,~~ ~~ultrasonic source,~~ noise nuisance, susceptible to external noise or acoustic vibration.

Electric energy / Electric fields

Leakage current - ~~earth leakage, enclosure leakage~~, leakage to accessories or other devices.
Magnetic fields – operating in a magnetic field or generates a magnetic field.
Static discharge – has materials which have a propensity to produce static discharge
Voltage / Current– hazardous AC and DC, AC and DC output sources

Mechanical / Kinetic energy/Potential (stored) energy -

~~Falling objects, high pressure fluid injection,~~ moving parts, vibrating parts, bending, compression, cutting, shearing, gravitational pull, suspended mass, tension, torsion, springs

Radiation energy

~~Ionizing radiation - accelerated particles (alpha particles, electrons, protons, neutrons). Gamma, x-ray~~
Non-ionizing radiation ~~– infrared, microwave, ultraviolet~~, laser, ~~other high power visible or electromagnetic field.~~

~~Thermal energy~~

~~Cryogenic effects~~

~~Hyperthermic effects~~

Biological agents

~~Bacteria, fungi, parasites, prions, toxins, viruses,~~

~~Chemical agents~~

~~Carcinogenic, mutagenic, reproductive, caustic, corrosive (acidic, alkaline, oxidants)~~

~~Flammable, combustible, explosive, fumes, vapours~~
~~Osmotic~~
~~Particles (including micro- and nanoparticles)~~
~~Pyrogenic~~
~~Solvents~~
~~Toxic – asbestos, heavy metals, inorganic or organic toxicants, silica~~

Immunological agents

Allergenic - antiseptic subs~~tances, latex, talc~~
~~Immunosuppressive~~
Irritants - cleaning residues
Sensitizing

Data

Access, non-availability, loss of confidentiality, inability to transfer, failure of data integrity.

~~**Delivery**~~

~~Quantity of flow, over or under delivery, incorrect or erratic rate, wrong mixture of chemical or gas or liquid.~~

Diagnostic information

Examination result lost or corrupt, image artefacts, ~~image orientation~~, image resolution, integrity of patient identity/information

Functionality

Alarm, critical performance, measurement, calibration, incorrect stated lifetime or limits of test acceptability.

Appendix 2

Table of Risk Probability Estimation

Probability	Score
Incredible **1:50 million - impossible chances**	0
Improbable **1:500 thousand - extremely remote**	1
Remote **1:5000 - not likely but definitely possible**	2
Occasional **1:50 - will occur quite often**	3
Probable **1:5 - expected regularly**	4
Frequent **1:1 - one or more during each use**	5

Risk Severity Estimation

Severity of Consequences	Score
Negligible **e.g. a scare, a loud bang**	0
Marginal **e.g. hitting thumb with hammer**	1
Significant **e.g. a cut requiring stitches**	2
Critical **e.g. a broken limb**	3
Catastrophic **e.g. death**	5
Major Disaster **e.g. multiple fatalities**	6

Note. The scores are such that any possibility of a risk producing even a rare catastrophic incident will automatically generate a minimum score of 4 and must be reviewed to define reduction measures. Remote but possible catastrophic risks will always generate a score of 9 or above and must be must be formally reviewed.

Risk Management Summary

Each risk noted to be evaluated, given an initial probability and severity. These two multiplied by each other give the initial risk. Control measures are then determined and the residual probability and severity are evaluated and these multiplied together to give the residual risk. If this residual risk is deemed acceptable then no other work needs to be carried out on the risk. If not further measures to be determined or the hazard or risk re-evaluated,

Hazard	Reason	IP	IS	IR	Control Measures	RP	RS	RR
Acoustic noise	The sample vibration system is noisy. Is the noise above recommended HSE levels? Hear damage to users or those constantly in the area when OCE being used.	5	2	10	1. The sample vibration system can be noisy so either fit quieter vibrator or ensure noise reduction foam is fitted. **2. Also need to check if the noise levels are within HSE guidelines.**	5	1	5
Weight	The power amplifier is about 5 Kg. Not secured to table. May fall off and cause injury.	2	3	6	1 Add note to user guide to inform to check power amp is positioned well on table. 2. If possible have power amp somehow fixed to the table.	1	3	3
Weight	The main body of the OCE is over 40Kg. Stability. If it were to topple over it could cause serious injury to anybody underneath it.	2	3	6	Perform tilt test. The unit is stable up to 20°. (Test required is not over tilt if placed at 10° from vertical. Test carried out at each side of unit.)	1	3	4
Weight	Mounting of both PC and Touchscreen. Secured and not able to fall off. Again a possible injury to anybody this assembly fell on.	3	2	6	Checked the PC and Touch screen are both assembled secured to the trolley.	1	2	2

Hazard	Reason	IP	IS	IR	Control Measures	RP	RS	RR
Motion	Are braked castors fitted to the OCE main body? Stop unit moving unattended or in use.	3	2	6	Check if braked castors fitted. If not have them fitted .	2	2	4
Motion	Braked castors fitted to the table for the power amplifier and signal generator. Stop unit moving unattended or in use.	3	2	6	Check if braked castors fitted. If not have them fitted.	2	2	4
Moving parts	Safety of motorised XYZ position controller for sample vibration system – finger trapping	2	2	4	Ensure that user instructions inform to take care when moving the XYZ position controller and the front cover is off. The movement is very slow hence persons should be able to move fingers out of the way before an injury occurs.	1	2	3
electrical / electricity	Check electrical layout. Wires coming loose and causing metal parts to carry currents. Electric shock risk	2	5	10	Electric shock if wiring becomes disconnect. R&D technicians have checked the wiring and connections. Rerouted and tidied up as required.	1	5	5
electrical / electricity	Current capabilities of the wiring. Incorrect current capabilities could lead to a fire.	2	5	10	Check wiring is rated correctly. R&D technicians have carried this out.	1	5	5

Hazard	Reason	IP	IS	IR	Control Measures	RP	RS	RR
Sample holder	Is it biocompatible with the biopsy sample? To ensure the sample is not degraded during scan and prior to sending to pathology for definitive checking.	5	5	25	Sample holder is made of laboratory grade glass. Hence yes.	0	0	0
Sample holder	Do the user instructions inform sample holder is single use only. Cross contamination between samples.	2	5	10	Check user instructions do state this – new sample holder for each new biopsy sample..	0	0	0
Sample holder	Does the sample holder material cause artefacts on the scanned image? Might cause a positive to be a negative or vice versa.	2	5	10	What testing done with the glass holders to check for this???			
User instructions	Contain all the relevant safety information and user instructions to ensure the use of the OCE does not cause harm to user or patient – via the end diagnosis.	3	5	15	Review of user information to 1. double check all the safety precautions included 2. scanning process and review fully detailed 3. actions to be taken if problems 4. contact details			

Hazard	Reason	IP	IS	IR	Control Measures	RP	RS	RR
User instructions	Contain cleaning instructions. If not clean correctly could cause OCE damage due to chemicals in incorrect cleaning materials. Cross contamination due to inadequate cleaning procedures.	2	3	6	Are these in the user information?			
Cleaning instructions	Reviewed by infection control to make sure OCE is reviewed for infection risks by experts.	2	3	6	Check if reviewed and ok			
Cleaning instructions	State clean after each use. Reduction of infection risks	2	3	6	Check if included			
Cleaning instructions	Detail the action to take if the sample or sample fluids falls into the OCE scanning area. IT is done correctly and no damage to the scanning systems.	2	3	6	Review the cleaning information to ensure this is covered.			

Hazard	Reason	IP	IS	IR	Control Measures	RP	RS	RR
User instructions	Only trained personnel to carry out repairs on the unit. Wrong service or repair can stop the unit from working or cause the scan data to give wrong results putting patient in danger.	3	5	15	Check user information for this warning. Plus is there a label on the OCE to this effect? See BS EN BS EN ISO 15223-1:2016	1	5	5
User instructions	electric shock risks exists inside the unit.	2	5	10	OCE Warning symbols and to be detailed in the user manual	1	5	5
User instructions	User instructions state no samples to be left inside the OCE after use? - Biological hazards to users	3	5	15	Check the OCE user manual to ensure that this is so. See the various standards for lab equipment.	1	5	5
User instructions	Device is not MRI compatible - magnetic fields	2	5	10	Make sure that the user instructions state the device not to be used in MRI area or field.	1	5	5
User instructions	Device is not to be used in an explosion risk area e.g. oxygen enriched, anaesthetic gases present.	2	5	10	User instructions to state this.	1	5	
Laser	Laser interlock required? Fitted. Reduce danger to eyes from laser energy.	3	3	9	Check and have non ionising safety officer check if all other warnings and precautions taken into account.	1	3	3
Labels	What ones are required? Third party check.	3	5	15	Review all labels and symbols are as expected. Check for any not attached to the OCE system.	1	5	5
User instructions	Details what the labels mean and where fitted? To make sure users understand what they mean.	3	5	15	lables – all explained in the user manual??.	1	5	5

Hazard	Reason	IP	IS	IR	Control Measures	RP	RS	RR
Interpretation of the scan result.	How have these been verified? To make sure the users understand what they are looking at when viewing a scan	3	5	15	Review of the verification and validation of the scanning checks and tests. Are these sufficient. What was actually done?	1	5	5
Scan result.	How to ensure results are correctly tag with the correct patient ID.	3	6	18	Review of the methods and storage of the results.	1	5	5
Scan result.	Data protection of results and patient details. Keeping information confidential	3	3	9	Is access to patient test results restricted or are the results saved such that they are secure from unauthorised access?	1	3	3
Device calibration/checking verification/validation	Optical coherence part – Does it work as intended specified and correctly?	2	5	10	Check the verification and validation testing to determine if the optical image is true and accurate.	1	5	5
Device calibration/checking verification/validation	Elastography part – working correctly and does it resolve the small differences in stiffness?	2	5	10	Need to ensure that the Elastography part is showing up differences in the stiffness inside the material….check on how this was achieved and what the min differences that can been seen and are these clinically relevant.	1	5	5
Enclosures and lids and things.	Enclosure fitted and secured during use especially when system used outside the laboratory setting.	2	5	10	User guide check to ensure states this is on, secured, clean	0	5	0

Appendix C5 6 Proposed control of academic work within M&H.

This is a draft of QP.03G. It is only intended for the purposes of this thesis.

0.1 General

Work carried out within Medical Physics and Hydatidiform Mole Follow-Up (Scotland), 'HMFUS', includes the following:
1. design, development and/or manufacture of medical devices, and in vitro diagnostic devices
2. creating new clinical testing methods and
3. providing bespoke services for a range of end users

These products may solely for 'in-house' use, passed to other users outside NHS Tayside or passed to 3rd parties for further development or manufacture.

This 'Product Realisation' procedure controls the work required to ensure these products:
1. fulfil customer needs
2. meet statutory or regulatory requirements
3. are fit for their intended use
4. have been fully risk assessed and all foreseeable risks in the use of these products have been reviewed and reduced to an acceptable level
5. have documentation including manufacturing and delivery requirements
6. undergo clinical testing as required which ensure results are accurate and fully validated
7. have documentation to describe services required or provided to meet customer needs
8. Most importantly, this procedure is developed to ensure that such products meet the requirements of UK and EU legislation relating to the design, development and manufacture of medical and in vitro diagnostic devices which are to be placed into service out with the legal entity know as NHS Tayside.

The word 'work' is used throughout this document to denote any task to develop or manufacture a new device, reagent, patient test, service or other item required by a customer, patient or NHS colleague.

Within the healthcare environment, various regulatory or statutory requirements, standards and professional guidelines must be adhered to. The product or service to be developed will determine which of these must be followed. For example a medical device might be controlled by UK statue 'The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019' or the equivalent EU regulation for Medical Device or In Vitro Diagnostic Device.

All work undertaken by academics or other 3rd parties, which might lead to a medical device, diagnostic test or service relating to the medical environment will have their initial project brief reviewed by the section head of R&D. The R&D section head or nominee will determine the level of control and hence documentation required during the project work. The documentation detailed in

QP.02A ‘Academic and 3rd Party Project Work’ will be completed at the start of such work and signed off by the Medical Physics project supervisor.

This procedure is based on BS EN ISO 13485:2016 standard and will use the applicable clauses of this standard for reference. Where areas of the 13485 standard are covered by the Medical Physics and Hydatidiform Mole Follow-Up (Scotland) Quality Manual, these areas will be referenced as required. Where these are not sufficient on their own, additional requirements will be detailed.

This procedure is not intended to control the design, development or manufacture of:
1. non-medical devices, services, tests, etc.
2. medical or in vitro diagnostic devices produced under the exemptions detailed in both the UK

Control of this work is detailed in QP.02 ‘Project and Product Realisation Work’.

This procedure is developed to ensure devices, products, services or modifications to medical devices or in vitro diagnostic devices meet the legislative or regulatory requirements of the following

1. UK Statue 2019 No. 791 Exiting The European Union Consumer Protection – The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 - Para 71 - Placing on the market and putting into service
2. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC - Article 5 Placing on the market and putting into service
3. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU - Article 5 Placing on the market and putting into service

0.2 Legal Entity

Medical Physics and Hydatidiform Mole Follow-Up (Scotland) are sections within NHS Tayside, part of NHS Scotland. These areas will be denoted as MP and HMFUS or referenced jointly as M&H.

0.3 Responsibility and authority

The QA team will ensure this procedure and other relevant documentation are adhered to as required.
M&H staff will ensure any changes to this procedure are flagged to the QA team or appropriate senior staff.
Senior staff will ensure that this procedure is implemented as required in their areas of responsibility.

1. Product Realisation Overview

The following 6 broad steps: Definition, Planning, Work, Testing, Review and Transfer will be carried out and some or all of these steps may need to be repeated once or several times during the project.

1. Definition – What is to be developed, realised, made, etc.
2. Planning – How we are going to produce the device, process, etc. including the producing the necessary outputs/paperwork to enable the idea to be used or made.
3. Work:

a) Research, Design and Development of a new product or modification to an existing product.

b) Producing an end product, i.e. item, service or test.

4. Testing – How to prove the device, process, service, etc. will:

a) Meet the needs of the users, patients and regulatory bodies.

b) Fulfil any specifications or constraints defined.

5. Review – To ensure the project is proceeding as expected, problems are address and any requested changes reviewed and responded to.
6. Transfer – If the work results in, for example, a product to be manufactured, a test to be put into clinical practice or a service for a customer, the documentation required for the end product to be delivered is known as the Transfer Documentation.

2. Scope of Product realisation

The areas of the BS EN ISO 13485:2016 standard which are not applicable to the work of MP and HMFUS are detailed in QM Section 1.5 Quality System Exclusions/Exemptions.

For reference these not applicable clauses are:

13485 Clause Description

7.5.3 Installation Activities - No medical devices require installation

7.5.5 Particular Requirements for Sterile Devices - No sterilisation undertaken.

7.5.7 Particular Requirements for Validation of Processes for Sterilisation and Sterile Barrier Systems -No sterilisation undertaken.

7.5.9.2 Particular Requirements for Implantable Medical Devices - No implantable devices are produced.

M&H will not act as importer or authorised representative.

3. References:

BS EN ISO 9001
BS EN ISO 13485
BS EN ISO 17025
BS EN ISO 15189
UK legislation relating to medical devices and in vitro diagnostic devices -
- 2019 No. 791 Exiting the European Union, Consumer Protection, The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019
EU regulations–
Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending ….etc.

Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices, amending….etc.

M&H Quality Manual and associated supporting documentation.
QP.01 CONTROL OF DOCUMENTATION AND DATA
QP.05 ORDERING, RECEIVING AND TRACEABILITY OF GOODS AND SERVICES
QP.06 CUSTOMER SPECIAL REQUIREMENTS
QP.08 CALIBRATION CONTROL
QP.10 CONTROL OF STANDARDS AND REGULATORY DOCUMENTATION
QP.11 SUPPLIER PERFORMANCE
QP.23 DISPOSAL OF SCRAP MATERIALS
QP.24 CONTROL OF RECORDS
QP.26 CUSTOMER SATISFACTION
QP.27 COMPETENCE, AWARENESS AND TRAINING
QP.29 INTERNAL AUDIT
QP.30 HANDLING / STORAGE
QP.31 DESPATCH/RECORD DOCUMENTATION
QP.35 POSITIVE RECALL PROCEDURE

The following work instruction have been developed to to assist in the documentation of the work. Their use will be highlighted in the body of this document.

WI-RD-01	EC Technical File Contents and Control
WI-RD-02	Labelling and Instructions for Use
WI-RD.03	Product Feedback
WI-RD-04	Competent Authority Notification
WI-RD-05	Risk Analysis
WI-RD-06	Medical Device Classification Rules
WI-RD-07	In Vitro Diagnostic Devices Classification Rules
WI-RD-10	IVDDR Essential Requirements Matrix
WI-RD-11	MDR Essential Requirements Matrix
WI-RD-12	Software Development

4. Quality Management System

4.1 General requirements

4.1.1 Overview of the system

This is detailed in the QM point 4.1.1 - Overview of the system with the following additions:
A full review of both the M&H QM and of this procedure will be undertaken in the event of the BS EN ISO 13485:2016 standard being revised. Changes to the standard will be incorporated as required to either the QM or this procedure.
Changes to applicable regulatory requirements or additional regulatory requirements will be reviewed and relevant documentation amended, produced or withdrawn as required
M&H will not act as importer or authorised representative.

4.1.2 Processes, their interaction and associated risk to the organisation

Any new processes required to enable product realisation will be requested via an Action Form (AF) See QP.20. The AF will detail:
1. the need for the new process;
2. how the new process interacts with other relevant parts of the QMS;
3. any risks associated with the introduction of this process and also any residual risks once the process has been implemented;
4. the risks associated if the proposed process is not introduced.

4.1.3 System Requirements

In addition to the details given in the QM 4.1.1 Overview of the System the need to demonstrate how this procedure and associated work conforms to the 13485:2016 standard is achieved via internal and external audits, review of AF's and any feedback relating to work undertaken or products resulting from this procedure.

4.1.4 Procedure and related process management

In addition to QM 4, which details the management of the QMS and the interaction of procedures and related processes. Any changes to the QMS impacting on this procedure or affecting the result of product realisation, whether this is a medical device, an in vitro device, a developed test in use, or a service provided to a third party, these changes will be managed in accordance with the requirements of BS EN ISO 13485 and relevant regulatory or statutory requirements.

4.1.5 Subcontracting

Responsibility for the conformity of any work outsourced to 3rd parties relating to this procedure will be retained by M&H.
As required by BS EN ISO 13485 M&H will retain responsibility for conformity to the standard, relevant regulatory, statutory requirements and customer

obligations for work undertaken by 3rd parties. Such 3rd party work will be monitored to ensure it meets agreed specification. The work will only commence once the capability of the 3rd party to undertake the work has been reviewed as satisfactory and the risks involved with using the 3rd party fully evaluated. A formal agreement of the required work shall be drawn up and signed. See also 7.4 of this procedure.

4.1.6 Software Validation

See QM 4.4 - Software Validation.

Note software validation or revalidation is controlled and documented as detailed in QP.01 and WI GEN 01.

4.2 Documentation requirements

4.2.1 General

As detailed in QM 4.2.1

4.2.2 Quality manual

As detailed in QM 4.2.2

4.2.3 Medical device file/Technical File

For product realisation work undertaken, a record will be maintained of the work carried out, even if this work does not come to a conclusion. The following information relating to the medical device, diagnostic test or service will be retained or referenced in the record:

1. A general description,
2. intended use/purpose,
3. specifications for product,
4. required labelling,
5. instructions for use, including user servicing, maintenance, calibration and disposal instructions as required,
6. service delivery agreement – these are agreements with 3rd parties for work carried out by Medical Physics e.g. maintenance of 3rd party hoists, repair and service of GP practice medical equipment, design and development activities, etc.,
7. full details of how the device is to be manufactured and tested prior to passing to customers/users,
8. device packaging, shipping, storage and handling during distribution and in use.
9. test details and how this testing meets the requirements of BS EN ISO 15189
10. output of reviews undertaken during the product realisation to ensure the various phases are progressing as planned, the work outputs are as required and any problems are resolved,

11. reviews of feedback from the users of devices, or services delivered to ensure they continue to meet requirements. If any problems are not resolved, the appropriate action, including reporting to relevant authorities is undertaken.

The following work instructions will be used to document legislative requirements and the production of the technical file content.

WI Reference	WI Title
WI-RD-01	EC Technical File Contents and Control
WI-RD-02	Labelling and Instructions for Use Requirements
WI-RD.03	Product Feedback
WI-RD-04	Competent Authority Notification
WI-RD-05	Risk Analysis
WI-RD-06	Medical Device Classification Rules
WI-RD-07	In Vitro Diagnostic Devices Classification Rules
WI-RD-08	IVDDR Manufacturing and Packaging Documentation
WI-RD-09	MDR Manufacturing and Packing Documentation
WI-RD-10	IVDDR Essential Requirements Matrix
WI-RD-11	MDR Essential Requirements Matrix

As detailed in Section 2 Scope of Product realisation the organisation does not carry out installation.

4.2.4 Control of documents
This is detailed in QM 4.2.3 and QP.01

4.2.5 Control of records

This is detailed in QM 4.2.4, QP.01 and QP.24.
QP.24 states that records relating to medical devices are maintained for the lifetime of the equipment plus 5 years.

5. Management responsibility

5.1 Management commitment
Detailed in QM 5.1

5.2 Customer focus
Detailed in QM 5.2.

5.3 Quality policy
The quality policy is detailed in QM 5.3

5.4 Planning

5.4.1 Quality objectives
See QM 5.4.1 plus related quality policies for areas within this quality system.

5.4.2 Quality management system planning
See QM 5.4.2

5.5 Responsibility, authority and communication

5.5.1 Responsibility and authority

See QM 5.1 and 5.5.1.

5.5.2 Management representative

See QM 5.5.2

5.5.3 Internal communication

See QM 5.5.3

5.6 Management review

5.6.1 General

See QM 5.6.1

5.6.2 Review input

All detailed in QM 5.6.2. To ensure full compliance with the requirements of BS EN 13485:2016, the following must be reviewed during the yearly cycle of Quality Review Meetings:

1. feedback from customers or users of medical devices , diagnostic tests and services to 3rd parties manufactured by M&H;
2. complaint handling related to work resulting from this procedure;
3. a review of any reports issued to regulatory authorities and actions arising;
4. the results of monitoring and measurement of processes – Are the processes associated with this procedure operating correctly and efficiently?
5. the results of monitoring and measurement of product – Do products or services meet their specification throughout the manufacturing process and at the point of use?
6. have any applicable new or revised regulatory or statutory requirements been issued– Why are they relevant and what is the plan for their introduction?

5.6.3 Review output

The review output will be formally recorded as detailed in QM 5.6.3. In the case of actions relating to this procedure, the record will include:

1. details of why changes are needed to the QMS to maintain the suitability, adequacy and effectiveness of the system and processes;
2. any improvements affecting customer or product stated requirements;
3. details of the action required to implement relevant new or revised regulatory or statutory requirements.

All actions resulting from quality review meetings will be documented on AF's (See QP.20). Time scales and staff responsible for implementing these actions will be detailed in the relevant AF.

6. Resource management

6.1 Provision of resources
See QM 6.1

6.2 Human resources
See QM 6.2 (6.2.1 and 6.2.2)

6.3 Infrastructure
Specifically for this procedure, the following requirements will be implemented. The infrastructure will be reviewed to ensure product requirements can be met and maintained. The infrastructure and environment are such that we ensure any manufactured product or items relating to the manufacturing process can be stored and handled appropriately without mix up between types, batches or any non-conforming product found.
Where maintenance of equipment required or services needed may affect the output of product realisation or end product quality, the risk associated with these activities will be documented. The results of risk mitigation will be reviewed and documented. Note equipment and services include – production equipment, test equipment, calibration standards, environment control system, power and IT systems.

6.4 Work environment and contamination control
See QM 6.4 with the additions detailed below.

6.4.1 Work environment
If special conditions are required for product realisation or production, these shall be documented. See also the requirements for BS EN ISO 15189 for the production of patient testing devices. These special conditions may be handling and storage of chemicals, parts, etc., the actual work environment or even the process equipment.
Health and Safety, PPE and special cleanliness or contamination prevention requirements will be documented. Staff, including temporary staff, working under these conditions will be trained in the use of PPE, how to work in any special environment and how to maintain appropriate cleanliness or contamination control.

6.4.2 Contamination control

In accordance with NHS Tayside Policy, the control of materials contaminated biologically or by hazardous waste, will be documented. The documentation will detail methods of segregation, disposal and control.
The arrangements to prevent contamination of product will be documented. This documentation will detail prevention of cross contamination, actions to be taken with product or items that do become contaminated, including storage until disposal. The documentation will detail action to be taken in the event of human or environment contamination. Where required appropriate decontamination equipment will be available. This can be in the form of chemical spill kits or washes. For the manufacture of patient testing devices the requirements of BS EN ISO 15189 must be adhered to in full.

7. Product realisation

This procedure covers the requirements to meet EU and UK legislation for Medical and In vitro Diagnostic devices being placed on the market or into service. QM 7 details the requirements of product realization for products, services or tests which do not require to be CE marked or are exempt from CE marking.
The following controls ensure the M&H QMS meets requirements of the BS EN ISO 13485:2016 standard, associated regulatory or statutory requirements and current industry practice and guidelines. In the case of IVDD device or laboratory patient testing the product realisation work must also meet the relevant requirements of BS EN ISO 15189.
Product realisation requirements:
1. full understanding of what is required;
2. document and review these requirements so they are fully understood and no unstated requirements remain undocumented – e.g. regulatory, statutory, product performance or special user needs;
3. the work to be undertaken is reviewed to ensure we can do this work. For example do we have the appropriate staff, facilities, procedures and processes in place to undertake the work?
4. the work is monitored to ensure it is proceeding as expected and the result of the work meets the requirements;
5. at the end of the product realisation we have full documentation to prove we have produced the required product, it meets requirements and we can replicate the product or service as and when required;
6. appropriate user instructions are produced.

The above is true for products in the design and development stages and also for customer requests for completed product. These products may be a new medical device, a new diagnostic test or a service provided to a third party.
All documentation or records will be retained or referenced in the design and development file/Technical File. Each design and development has a unique job/work reference or batch number. For example clinical engineering this is the e-Quip job number and for HMFUS this is HMFUS Tech File 01, 02, etc.

7.2 Planning of product realisation

Each new product realisation request is risk assessed to ensure any risks associated with the new work are informed to appropriate management. Organisational risks must be passed to the head of the appropriated service.
A review will be carried out prior to new product realisation work to ensure that current procedures, processes (work instructions, protocols or standard operating protocols) are adequate for the work to be undertaken. If required, an action plan to produce required documentation will be drawn up. The action will also detail how the documentation will be risk assessed to ensure consistency with the current QMS.
Planning of product realisation will be documented per this quality management system. ???The level of documentation will be appropriate to the work required or the type of product being realised. The following points will be assessed and documented as required.
1. customer requirements,

2. the need for the work and any particular objectives for the output of the product realisation.
3. regulatory and statutory requirements,
4. special technical or intended user requirements (is the user trained, disabled, a career, etc.),
5. if a diagnostic test, specific requirements under the current BS EN ISO 15189 standard.
6. how to monitor the progress of the work,
7. foreseen requirements for any measurement, inspection and test – work stages or final product
8. special handling, storage and distribution.
9. special traceability requirements of the final product or items used in the manufacture or the product.
10. details of required product verification and validation and when to carry these out.
11. details of how the final product will be checked to ensure it meets documented requirements.

Risk assessment of product realisation work should reference ISO 14971 and WI-RD 05 'Risk Analysis'

7.3 Customer-related processes

7.3.1 Determination of requirements related to product

Prior to agreeing to a customer request M&H will ensure they fully understand and document the customer requirements. These include

1. the customer requirements, including the volume required, special instructions regarding delivery of product or service, if a site visit is request post-delivery actives including technical/specialist training, test report layouts and billing arrangements,
2. requirements not specified by the customer but required to ensure product meets customer or user requirements, include determining the clinical context for patient testing or sample analysis,
3. regulatory or statutory requirements related to the product to ensure it can be delivered,
4. user training to ensure correct and safe operation of the product,
5. additional requirements imposed by M&H or NHS Tayside management.

7.3.2 Review of requirements related to product

Prior to delivery of product or fulfilment of a work request, whether this product is an item, test or service, a review will be conducted to ensure that:

1. the documented product or work requirements or specification are reviewed to ensure they are understood and agreed by all interested parties,
2. the specified regulatory, statutory, professional and industry standard requirements have been met,
3. identified user or customer training is planned or available,
4. M&H have the staff and infrastructure to meet the stated requirements or customer request,
5. the original requirements or request are reviewed to ensure they have not changed. If they have, a review of the changes must be undertaken to ensure these

changes can be accommodated. This review must be undertaken for repeat orders or work requests.
The results of the review and any actions arising will be documented and maintained as per this QMS.
Where no customer requirements are stated, M&H will determine relevant requirements and agree these with the customer prior to fulfilling requests.
When product requirements are changed, the organization shall ensure that relevant documents are amended and that relevant personnel are made aware of the changed requirements.
7.3.3 Communication
M&H will ensure customers are kept informed of;
1. the progress of customer complaints or feedback given. See QP.20 and QP.26
2. the progress of customer enquiries, contracts or amendments to requests or requirements. See QP.20,
3. new products, services or tests which might be of interest to the customer,
4. advisory Notices. See QP.35. QP.35 also details communication with relevant regulatory and statutory authorities.

7.4 Design and development

7.4.1 General
This procedure, related Work Instructions and relevant BS EN ISO 15189 protocols and Standard Operating Procedures document the requirements of design and development and any documentation to be produced at each stage of the work, this documentation will include all the information required to produce a device, carry out a diagnostic test or carry out work for a 3rd party.
7.4.2 Design and development planning
Each design and development activity is planned and those responsible for activity are identified. The plans are reviewed and updated as the work evolves. The plans will detail the review, validation and verification requirements necessary for the various design and development activities. Planning documentation will be retained with the work documentation. The plans will also include identification of organisational and technical interfaces between the different groups within M&H. The plans will be reviewed and updated as the design and development work evolves
Planning documentation will include:
1. The required design and development stages needed to produce the product.
2. Identification of the responsibility and authority for the design and development stages/activities.
3. Resource required.
4. Special staff training/competence.
5. Verification, validation and transfer activities between one stage and the next.
6. How transfer activities are monitored to ensure the outputs from one stage are correctly transferred to the next.
Transfer activity - how information, parts or other items are passed between design and development stages. This enables the output of one stage/activity to be

correctly passed to a second stage/activity for design and development input. For example, the final transfer activity for a product encompasses all the information to enable the product to be manufactured.

7.4.3 Design and development inputs

Design and development inputs define the product. If a product is complex and requires many design and development stages or activities, these inputs may be required to enable a design and development stage or activity to start. Design and development inputs will be documented and reviewed to ensure they are adequate and well defined. How the inputs can be verified and validated will also be documented. Design and development inputs must not conflict.
For an overall product these inputs will include:
1. Applicable specified regulatory, statutory, professional and industry standard guidelines or requirements.
2. List of standards, national or international, to be adhered to or met.
3. Details of other similar devices, products or patient tests which may enable better understanding of the actual work to be carried out.
4. The nature of the end user or the environment the product will be used in.
5. Details of foreseen risks or results of risk assessments carried out,specially the result of risk assessments carried out in the planning stage.
6. Any special storage or protection requirements for items used in the design and development activities,
7. Details of the expected outcome of the design and development work:
a) for a product then functionality, performance, usability, physical properties, special training requirements, target market, if professional or general public, complexity of user guide and safety requirements.
b) for a patient test then the pass fail criteria, type of equipment required to undertake the testing, level of competence of intended user – professional or general public, required user guide and disposal information.
c) for a 3rd party service – staffing required, equipment population, locality of the work, reporting and invoicing methods and type of contractual agreement required.
8. For design and development work with interrelated activities or stages, the inputs to each stage will depend on the output of previous stages. These outputs could be a software application, a mechanical or electric module, a completed scientific study, or the results of a clinical trial. These outputs must be defined, have levels of acceptability and be documented. Stage/activities should only commence after these inputs (or outputs from the previous stage) have been reviewed and deemed acceptable.
9. Traceability requirements of the product, materials, parts or items used, monitoring of production and calibration equipment, etc.
10. Other design and development inputs may also be documented.

See also IEC 62366–1.

7.4.4 Design and development outputs

Documentation of the design and development activity will be maintained. This documentation will include detailed records of any research, design and development and testing carried out. The outputs of design and development shall

be in a form suitable for verification against the inputs. Any disparity between the outputs and inputs will be reviewed and resolved.
These outputs will only be released for use once reviewed and accepted.
Design output shall:
1. meet the requirements detailed in 7.3.3 Design and development inputs – for the overall project and for each activity or stage;
2. enable the product to be manufactured or supplied, patient or sample test to be put into use or the 3rd party service carried out. This can include purchasing information, production and assembly information and schedules of work;
3. contain or reference product acceptance criteria;
4. contain or reference the protection of materials or parts used during the manufacture of product, the product itself while in storage or while shipping product or components parts;
5. identify those characteristics of the final product that are crucial to the safe and proper operation of the product.
Other outputs may be required or defined.

7.4.5 Design and development review

Reviews are held to check that the design and development activities are meeting the input requirements. Actions are proposed to resolve any problems identified during these reviews. The reviews are held as detailed in the design and development plan, 7.3.2, or as required by those managing the work.
Reviews will be carried out by staff knowledgeable and/or expert in the work being reviewed. Records of such reviews will be held or referenced in the design and development file/Technical File

7.4.6 Design and development verification

• Verification: Did we design or produce the device correctly? Does it work the way it is supposed to? Does it meet technical or scientific specification? Did the offered service meet the contractual specification?
The definition of verification is the act of determining whether a product or service can meet a specific requirement. One of the most critical and fundamental components of product creation includes ensuring the product will perform as intended.
This stage ensures that the design output meets the design input requirements. Have we produced an item that meets it technical, scientific, regulatory, quantifiable requirements defined in the design and development input?
Verification activities or reviews will be carried out as planned and be documented. These verification activities can include:
a) holding and recording design reviews;
b) undertaking qualification tests or functional design testing and demonstrations;
c) comparing the new design with similar proven designs, if available;
d) if the product is intended to work in combination with other products, verification will also be carried out in these intended combinations,
e) carrying out clinical investigations and trials.

7.4.7 Design and development validation

• Design Validation: Did you design the correct device? Did we make what the customer wanted? Is this what was intended at the start of the design and development activity or have we ended up answering a different question? According to the American Society for Quality, the definition of validation in a quality environment is the act of confirming that a product or service meets the need for which it was created.

Design validation tests are used to ensure that the product/service meets the customers' application or intended use. Validation testing can include environmental and emissions testing, customer/patient acceptance checks and further clinical investigations and trials. Validation activities will be documented. The documentation will include the validation plans, methods of testing and the pass fail criteria for tests carried out.

Depending on the type and nature of the product statistically valid sample sizes will be required when conducting validation testing. How the samples are chosen and the sample size determined will also be documented.

Where required clinical evaluations or performance evaluations of the device will be carried out in accordance with relevant regulatory and statutory requirements or as required by professional body guidelines. Note: devices used for such clinical or performance evaluations are not to be passed for customer use.

If the product is intended to be used in combination with other products then validation will also be carried out with these intended combinations.

Validation shall be completed prior to release for use of the product to the customer.

7.4.8 Design and development transfer

The results of design and development work will need to be documented, reviewed and verified to enable, for example, a product to be produced, a diagnostic test to be put into practice or a service to be delivered. The contents of design and development transfer documentation will be varied.

The following are examples of design and development transfer documentation.

1. For a device, the documentation will contain sufficient detail for the device to be manufactured, tested, packaged and shipped/passed to the end user/customer. The documentation includes as required:

a) Assembly and layout drawings, schematics and final software required, parts lists along with supplier details and special material or component requirements.

b) Details of manufacturing steps,

c) Identification of manufacturing status or stage,

d) Module or component testing, assembly checks and final calibration methods and pass fail criteria. Documentation of results and production of relevant certificates.

e) User instructions and labels and labelling instructions

f) Packaging and transport details.

g) Device identification , UDI, or traceability,

h) Any other details required to ensure the device is manufactured and shipped to a customer such that it functions as expected.

2. For a test kit or constituent part:

a) the instructions to enable the kit/part to be manufactured;

b) The limits of acceptability, the validation and verification details of each component part of the kit, limits of acceptability and final test methods;

c) Details of chemicals, constituent parts or other materials, their suppliers and any special supplier material or component requirements;
d) Identification of manufacturing status or stage,
e) User instructions and labels and labelling instructions
f) Packaging and transport details.
g) Device identification , UDI, or traceability,
h) Results of a review that the product can be manufactured as envisaged – in house, subcontract, etc,
i) Any other details required to ensure the test kit or part is manufactured and shipped to a customer such that it performs as expected.

3. A new diagnostic test will require protocols to detail
a) how the test is to be performed, outcomes expected and how to documented test results.,
b) Interpretation of results – both clinically and in lay terms if deemed necessary.
c) Equipment to be used, and, if required how calibrated and operated.
d) Testing environment,
e) Any other details required to ensure the test kit or part is manufactured and shipped to a customer such that it performs as expected.
4. A new service
a) The required work and any special methods to be employed,
b) The required level of service,
c) Where the work is to be performed,
d) Financial arrangements
e) Reporting arrangements
f) Service review arrangements.
g) If this is a service accepted on behalf of NHS Scotland the agreement between NHS Tayside and NHS Scotland will detail the service arrangements.

7.4.9 Control of design and development changes

Changes to the agreed design and development including plans, input or output requirements, validation or verification requirements, shall be identified, documented and approved using the Q-Pulse to raise an AF according to QP.20. Changes will be reviewed to determine how they may have or will affect the design and development. Changes will also be reviewed to determine their impact on completed design and development tasks, items already in the post design and development phase including products, tests or services already in use.
The review should include the impact to performance, characteristic, usability and safety. What affect has the change made to services already performed or to products delivered or tests performed?
Most importantly any changes to regulatory or statutory requirements or the intended use of a device or patient test will be highlighted and the requested change reviewed with the customer, relevant senior staff and a member of the QA team.
Prior to accepting and implementing a design change it will be reviewed, verified, validated, approved, appropriate documentation produced or amended to enable the change to be implemented and communicated as to relevant staff, user groups, required relevant authorities or professional bodies.

7.4.10 Design and development files

The information and documentation produced during the design and development work is retained either in one file or referenced in a master file. This information and documentation will include details showing how conformity to the design and development inputs was achieved and any changes reviewed whether implemented or not. This file will also reference the location of any technical file or technical documentation produced to fulfil regulatory or statutory requirements.

7.5 Purchasing

QP.05 - Ordering, Receiving and Traceability of Goods and Services, describes the process of ordering goods and services within NHS Tayside.

7.5.1 Purchasing process

See QM 7.4.1 with the following addition:

1. Consideration must be given to the risk a particular supplier may have on product realisation.
2. Delivered product non-conformance or delivery missed or out with stipulated delivery requirements will be one method used in the ongoing evaluation suppliers
3. Supplier non-conformance will be evaluated on the risk associated with the non-conformance.

See also QP.20 and QP.11

7.5.2 Purchasing information

See QM 7.4.2 with the following additions:

1. Design and development documentation and transfer documentation will detail any special product acceptance requirements e.g. acceptance procedures, equipment – for handling or testing of purchased product, special storage needs, etc.
2. Details of any specialist qualifications or training required by the supplier's staff,
3. Agreed certification to supply specialist materials.
4. Prior notice to the supplier of materials which require certificates of conformance or material history/provenance.
5. Prior to placing orders with a new supplier, special requirements will be documented and agreed.
6. Changes to agreed product specification will be notified ASAP by the supplier to relevant M&H staff or by M&H staff to the supplier.
7. Purchasing information will be reviewed prior to authorising orders.

7.5.3 Verification of purchased product

See QM 7.4.3 with the addition of:

A formal review will be held to determine the effect of any delivered products which are found to be outside the required purchasing specification may have had to either product delivered to customers, undergoing manufacture or to the outcome of design and development activities or stages.

7.6 Production and service provision

This section relates to any activity to produce an end product, have this product delivered to the customer and ensure the customer can use the product. Further the

section also relates to any related services provided to the customer, including invoicing, finance, repair or service of equipment, supply and management of work for NHS Scotland or others – GP practices, health centres, etc.
This section details the controls to ensure we provide products e.g. medical devices, patient test, 3rd party services under controlled conditions and that the ancillary activities to ensure this happens are similarly controlled and documented.

7.6.1 Control of production and service provision

See QM 7.5.1 with the following additions:

1. Will the envisaged infrastructure and environment:

a) be suitable for manufacture of the product?

b) not harm the end product?

c) allow it to support customer or internal services to be fulfilled?

2. Where required, document the checking and measurement of process parameters and product characteristics;

3. Ensure that labelling and packaging instructions are clearly defined;

4. Determine the activities for product release and delivery (e.g. specialist transport or handling)

5. If required, determine and document post-delivery activities including training, calibration and implementation of service schedules.

6. For all physical products or tests, the level of product traceability required and how this is controlled will be documented.

7.6.2 Cleanliness of product

Any special cleaning or contamination control requirements will be documented. Documentation will be produced if:

1. Cleaning or decontamination of the device, its constituent modules, assemblies or materials will occur during the manufacturing processes,

2. The product requires special cleaning prior to use but is not to be sterilised,

3. The product is supplied non-sterile but must be cleaned prior to sterilization or use,

4. The product is supplied clean prior to sterilisation or use,

5. The product is supplied unclean, but it must be cleaned or sterilised prior to use.

7.6.3 Installation activities

No product installation is undertaken under this QMS. Installation in this case relates to providing instructions for the installation of product, providing building or infrastructure requirements.

7.6.4 Servicing activities

See QM 7.5.1 a, b and c with the following additions:
Servicing Activities
If servicing activities are required by the customer, the organization must document the servicing procedures, reference materials, and reference measurements for performing servicing activities and ensuring product requirements relating to this activity are met.
Where a product requires servicing or calibration to ensure it is fit for use, these activities will be documented in either the user instructions or a separate specialist technical manual. This information will detail the appropriate servicing,

calibration or final test/pre use procedures, any required materials, reference measurements, special tools or instruments and the acceptable pass/ fail criteria. Analyses of M&H, users or suppliers feedback of such servicing or calibration activities will be undertaken. The output from this analysis should be used to:

1. Instigate product improvement;
2. Inform if a review of service/calibration activities to be undertaken;
3. Instigate a review of service or calibration intervals;
4. Determine if a customer complaint should be raised.

7.6.5 Particular requirements for sterile medical devices

For devices requiring sterilisation or special cleaning prior to use or delivery, only 3rd party approved and documented processes will be used. This will be documentation as 7.5.2 ‘Cleanliness of product’ above.

7.6.6 Validation of processes for production and service provision

Validation of process for production and service provision

Process validation is required when you are not able to verify the output of a process afterwards, so that problems only become apparent during product or service use. When this is the case, you validate your process to make sure it achieves the planned results and this is, of course, very specific to the processes in the company. ???

Processes, including servicing, which cannot be verified by inspection or testing and where deficiencies in such processes might become apparent after a period of time, shall be documented. The documentation shall include the qualification of the personnel, equipment to be used, specific methods, criteria for end of process or work acceptance, procedures of work and record keeping required.

These types of processes will be validated/tested to demonstrate reliable process outcomes. Any statistical techniques used will be documented and rational for their use, including choice of sample sizes, given.

The process and relevant documentation will have scheduled review to ensure it remains fit for purpose.

Following changes to the process, equipment or material specification, the process and associated documentation must be reviewed and if required revalidated.

Control and maintenance of computer software used in the testing and/or inspection of work carried out will be documented. Pre-use validation and revalidation, if software is updated or modified, shall be proportionate to the risk associated with the use of the software, including the effect on the ability of the product to conform to specifications. See also QM 4.4, QP.01 and WI???

7.6.7 Particular requirements for validation of processes for sterilization **and** sterile barrier systems

No Sterilisation processes are undertaken under this QMS. For devices requiring sterilisation or special cleaning prior to use or delivery, only 3rd party appropriately approved and documented processes will be used.

7.6.8 Identification

See also QM 7.3.5 and QP.05

HMFUS assign Starting Material Numbers to identify the product and associated materials and items during production, as appropriate. Product traceability is maintained by recording these in quality documents where applicable. The production paperwork will be followed at all times and signed off as each activity is accomplished. This allows the status of the product, including the monitoring and measurements status, to be known at all times during production.

Clinical Engineering assign a unique e-Quip work number to all new work. This number identifies the product. All items or paper work used in the production of a device is referenced by this number. The various tasks to be undertaken and their sequence are documented in the manufacturing documentation. Staff will follow the work sequence as detailed in the manufacturing document, they enter the work they have carried out into the-Quip system. They will also record any monitoring and measurement undertaken as required, either directly into the e-Quip system or into designated forms.
Each medical product will be identified as detailed in the design and development transfer documentation. HMFUS products are given product batch numbers as detailed in HMFUS production documentation and for Clinical Engineering, each product is given a Serial number and requires a UDI as detailed in Clinical Engineering production documentation.
Products returned for inspection, review, rework or otherwise will be labelled with a non-conformance hold label, see QP.20, The non-conformance hold label will be retained with the product until the required action to deal with the product has been established and carried out.
See also 7.3.8 Design and development transfer above.

7.6.9 Traceability

7.5.9.1 General

.
QM 7.3.5 and in particular procedure QP.05 details the tractability requirements for all areas covered by the QMS. Additionally the design and development inputs include a requirement for traceability and recording of traceability to be in accordance with the relevant regulatory, statutory, professional or industry requirements. See 7.3.3 Design and development inputs above.
7.5.9.2 Particular requirements for implantable medical devices
No implantable devices are manufactured by M&H and hence are not within the scope of this QMS

7.6.10 Customer property

Customer supplied property for the use or incorporation into the manufacture of product will be treated as per QM 7.5.4.
7.6.11 Preservation of product
See QM 7.5.5 with the additional requirement:
Any special requirements regarding the protection of items used in the design and development of product, the manufacture of product or while shipping product or components parts will be documented in the transfer documentation,

7.7 Control of monitoring and measuring equipment

The following additional requirements to QM 7.6, QP.08 and associated instructions will be followed:
1. Special monitoring and measurement required to ensure end product requirements are achieved will be documented;
2. If no national or international standards exist, documented reasoning for the method of calibration and verification of the monitoring or measurement will be produced;
3. The need for any adjustments or readjustments will be recorded;

4. Such equipment or materials to be protected from harm, deterioration, contamination or inadvertent adjustment will be identified;
5. when monitoring or measurement devices or standards are found to be in error, the validity of previous results using these devices or standards will be reviewed and assessed to determine the effect of the error has been on the work undertaken, in progress or any released products. (Product already issued may need to be recalled see QP.35)
6. computer software or applications used will be validated or revalidate prior to use. The actual validation or revalidation undertaken will be proportionate to the risk the software poses to this QMS and to M&H. See also QM 4.4, and WI……

8. Measurement, analysis and improvement

8.1 General

The requirements given in QM 8.1 will be extended to demonstrate conformity of product and the provisions detailed in 7.5 Production and service provision of this procedure.

All the elements of QM 8.2 apply and the following additional requirements:

8.2.1 Feedback

Feedback is controlled and documented as detailed in QP.26 and QP.20. Feedback is an agenda item for the QMS review. For the specific requirements of this procedure, feedback will include reports relating to product, manufacturing and service.

8.2.2 Complaint handling

Complaint handling is detailed in QP.26 and QP.20. Feedback is reviewed to determine:

1. if a complaint should be raised on behalf of a customer;
2. if regulatory or statutory reporting is required;
3. the action to be taken with problems related to product;
4. the reasons for not investigating an incident - this must be documented on the relevant AF;
5. if subcontractors or other 3rd parties are involved – they must be included in complaint investigation or review.

8.2.3 Reporting to regulatory authorities

QP.35 details positive recall and reporting to regulatory or statutory authorities.

8.2.4 Internal audit

QM 8.2.2 details the requirements in relation to audits while QP.29 is the control procedure for internal audits. All audits, internal or external, are recorded in Q-Pulse.

8.2.5 Monitoring and measurement of processes

See QM 8.2.3

8.2.6 Monitoring and measurement of product

See QM 8.2.4. Monitoring and measurement for each product is detailed in the transfer documents, 7.3.8 Design and development transfer. Only after appropriate review and sign off will product be available for issue or a service put into use.

8.3 Control of nonconforming product

The requirements of QM 8.3 and QP.20 apply to this section with the following additions:

8.3.1 General

When non-conforming products or services are found or an action taken to prevent a possible non-conformance, an AF will be raised (See QP.20). The non-conformance or possible non-conformance will be detailed in the …. Section and the AF passed to the appropriate member of staff to detail action to resolve the problem.

8.3.2 Actions in response to non-conforming product detected before delivery

The following actions in response to non-conforming product detected before delivery or a non-conforming services found prior to being put into use may be undertaken:

1. Carrying out required action to remove the non-conformity
2. Removing the product or stopping the service from being put into use
3. Authorising a concession for :

a) use,
b) product release, or
c) acceptance for use if an item or part used in the manufacturing process.

4. Authorising a concession for the service to be used.

Concessions will be requested via an AF. Those reviewing concessions will need to demonstrate regulatory or statutory requirements are being adhered to and justify the granting of the concession.

8.3.3 Actions in response to non-conforming product detected after delivery

When product or services are found to be non-conforming after they have been put into use or service a full review of the consequences will be undertaken. The results of the review will be retained in an AF. The nature of any recall action will depend on the results of the review. QP35 details recall and notification of medical device regulator authority.

8.3.4 Rework

Rework to bring a product up to specified requirement will be documented. This may be simple instructions appended to the AF related to the non-conformance or, for more complex rework activities, a rework instruction will be drawn up and issued in accordance to QP.01.

For services requiring to be modified to ensure they meet requirements the documentation will documented in the AF related to the non-conformance.

8.4 Analysis of data

QM 8.4 details the general analysis of data used to ensure the QMS, procedures and related documentation are effective and that product or services produced or provided are meeting requirements.

8.5 Improvement

The following requirements are in addition to those given in QM 8.5:

8.5.1 General

In addition to QM 8.5.1 the following information will be used to highlight areas of improvement to the quality management system, related documentation and to ensure the safety of medical devices produced.

1. data from post market surveillance,
2. corrective actions,
3. preventive actions,
4. the use of concessions relating to non-conforming product or services,

8.5.2 Corrective action

QM 8.5.2 and QP.20. QP.20 details the control of corrective actions. The following are in addition the requirements of QP.20 for work controlled by this procedure control. Such work includes:

1. medical product or related service realisation;
2. medical device or related service design and development,
3. manufacture of medical or related product,
4. delivery of service related to medical product
5. procedures, process and documentation related to this work.

Corrective action is used to describe any action to remove an error or problem found within the QMS or during the manufacturing/production of a product or a problem found or reported with a completed product or service.

Such problems will be documented using the Q-Pulse AF

The ‘Details’ section will be a description of the problem or error.

The ‘Action Required’ section will be completed by the relevant senior staff and will detail

9. the root cause/reason the problem/non-conformance occurred andthe action plan, including required documentation to clear the problem or non-conformance and prevent it from reoccurring.

The ‘review action taken’ section will be completed by the QSM or nominee in conjunction with relevant senior staff who will determine if:

1. the problem/non-conformance been reviewed correctly and is the root cause/reason adequate;
2. the action plan detailed has cleared the problem/non-conformance;
3. the action plan ensures the problem/non-conformance does not reoccur; it is correct and effective;
4. the above action plan has not had any adverse effect on the QMS, the product or service requirements or safety or any resultant device.

The above process will also be implemented for complaints raised against work controlled by this procedure.

8.5.3 Preventive action

QM 8.5.3 and QP.20.

QP.20 details how the prevention of potential non-conformities, possible deviation from specified requirements, errors relating to work or other possible risks. Preventative action can be proactive, for example staff training, outputs from quality review meeting, PPM schedules for critical equipment, review of supplier errors, review of procedures and related documentation relating to the work, customer feedback review and internal and external audits.

Preventable actions may be the results of audit findings, staff suggestions or trend analysis.

The following relates to areas where specific preventative actions need to be undertaken:

1. medical product or related service realisation;
2. medical device or related service design and development,
3. manufacture of medical or related product,
4. delivery of service related to medical product, or
5. procedures, processes and documentation affecting work related to this procedure.

Action Forms as detailed in QP.20 shall be used to document the preventative action as follows.

The ‘Details’ section will be a description of the possible problem or preventative action.

The ‘Action Required’ section will be completed by the relevant senior staff and will detail

1. the risk to the QMS if the possible problem is not resolved or the preventative action is not implemented.
2. the action plan, including required documentation to remove the possible problem or instigate the preventable action.

The ‘review action taken’ section will be completed by the QSM or nominee in conjunction with relevant senior staff who will determine if:

1. the possible problem or preventative action been reviewed correctly and if the risk to the QMS been defined appropriately;
2. the action plan was sufficient;
3. the action plan ensures the possibility of the problem occurring has been removed and the preventative action is correct and effective;
4. the above action plan has not had any adverse effect on the QMS, the product or service requirements or safety or any resultant device.

The above process will also be implemented when, after initial review, customer feedback is deemed as a possible complaint.

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